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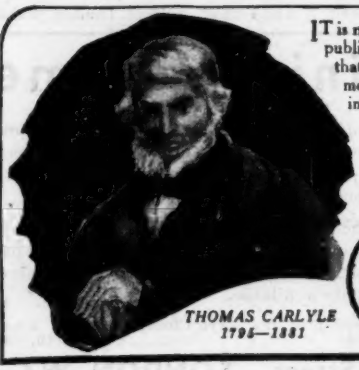

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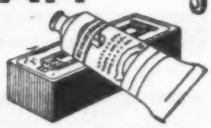

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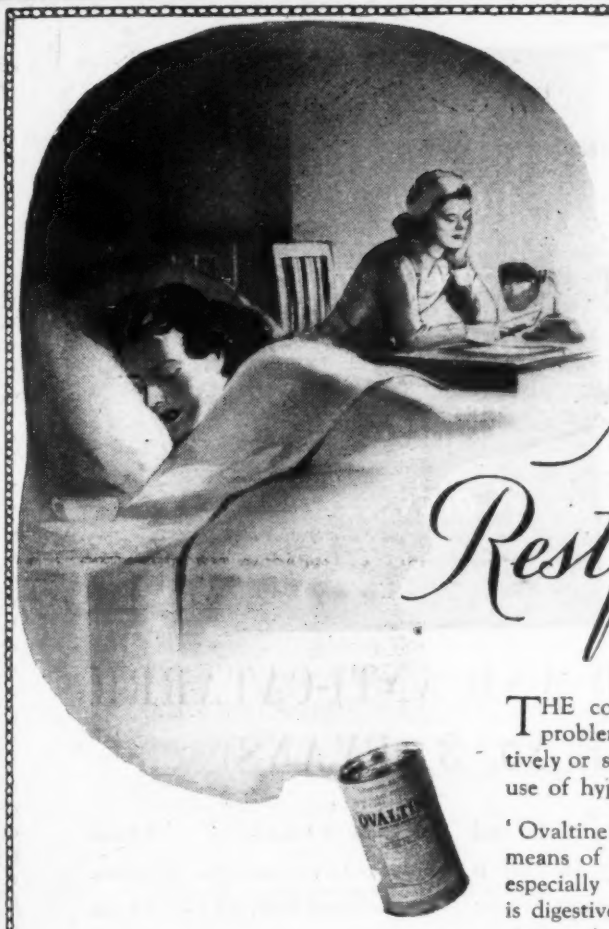

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MASS ASPHYXIA

MEDICAL ASPECTS OF THE TUBE SHELTER DISASTER

KEITH SIMPSON, M D LOND
ASSISTANT LECTURER IN FORENSIC MEDICINE, GUY'S HOSPITAL

DURING the evening of March 3, 1943, an alert was sounded in the central London area. No enemy action had as yet taken place when people began to arrive in large numbers at a tube shelter, and although, some 5 minutes later, several hundred were congregated at the single entrance and passing down the first flight of stairs "there was no crowding and the people were moving quite freely . . . coming down" (according to a witness who stood facing them on the landing of the second flight of stairs and had an uninterrupted view) "in an orderly manner."[1] There was however a steady thrust from behind which may have pressed on those in front who were picking their way—often with children—down stairs lit with dimmed lighting. The entrance to the shelter was 10 ft. wide and opened direct on a stairway of 19 steps leading to a first landing of 15 ft. by 10 ft. A second flight of stairs followed at right-angles to the first, 6 steps 10 ft. 3. in. wide leading to the booking-hall. A 57 step escalator led out of this to the rail level. There was no lack of accommodation, shelter being provided for 10,000 people, including 5000 in bunks. Only some 2000 were then in the shelter, and those using it knew that its accommodation had not on any occasion been taxed; there would be room for all.

About ten minutes after the alert signal there was a loud bang. According to two witnesses still outside the shelter, "there was a crush at the entrance" but "no panic or stampede." Indeed the people then at the entrance were either "carried inside by the people pushing behind" or "just stuck." "There was no movement of the people in front" and "it seemed as if they had been blocked by something." They had indeed, for a tragic little incident had occurred on the first flight of stairs. "The crowd was coming down still orderly" according to the first witness quoted, the man on the second landing, when he saw "a woman, who was holding a little girl by the hand, fall down. As she did so she sort of pulled the child with her and they both fell on to the bottom step." As soon as she and the child fell a man who was on her left also fell down. "The people behind did not stop but continued to come down on to the landing. Within seconds of these persons falling other people had fallen on top of them and they piled up to 3 or 4 feet high. There was a lot of screaming and shouting but it was then impossible for any person to extricate himself or herself. The persons thus became jammed on the first flight of stairs. There were none lying on the landing." This witness "tried to pull the people from the steps but they were jammed too tightly." Wardens could not pull anyone out until the pressure of those who stood behind on the stairs had been relieved. One of these said in evidence that she, with her children, "was pushed on top of them," and other people came forward on top of her. Another said, "The pressure was very heavy and we were unable to move as much as a finger. No person could move either backwards or forwards."

A police constable in plain clothes, who was taking his family into the shelter, realised the impasse and had to climb over the mass of entangled and tightly compressed people to reach the landing. He said, "I realised I could not do anything myself so I climbed back over the people to the entrance again." Help was hurriedly summoned, and when after some 10 minutes, the pressure from behind had been relieved, victims were pulled by main force from the surface of the mass. Further messages for assistance arrived at the local police-stations, and within 15 minutes of the incident occurring several groups of police officers were already at work. A senior officer spoke of "at least 200 people piled in a tightly wedged heap on the lower half of the first flight of stone steps leading from street level." For the next hour rescue work proceeded tediously, the conditions impeding rapid extraction of people. At the end of that time a sub-divisional police inspector still had to "scramble over the pile of trapped persons" to reach the bottom of the first flight of stairs. All casualties had been cleared within 3 hours of the incident. In addition to wardens, a chief inspector of police, 2 subdivisional, one station and 2 other inspectors, 6 sergeants and 60 constables were hard at work during this period. The ventilation of the stairway remained adequate throughout.

In all, 161 persons were dead when extricated, and a further 12 died after admission to local hospitals. Of these 173 who died, 28 were men, 83 women, and 62 children under the age of sixteen; 43 other persons who were admitted as inpatients to the local hospitals made complete recoveries and were discharged. In addition a large number received minor attention but were not detained.

A subdivisional inspector describing the extrication of victims said, "Almost the last person removed from the bottom was a girl of about seven years. She stood up and walked to the first-aid post unaided. It made no difference what position they occupied in the pile whether people were living or dead. Some of the top ones were obviously dead and some at the bottom were living." No fractures were found, and the patients admitted to hospital showed in general only soft crushing injuries of varying weight and surface abrasions. A group of cases which developed the crush syndrome with myohæmoglobinuria, as described in this country by Bywaters, were studied by him during their convalescence. Independent observation of a similar change was made at the first autopsy in a subject aged eighteen years, and material was submitted to Bywaters from this case.

The entire group of deaths were reported to the coroner for the district, and on his instructions four selected autopsies were made; the details of these are set out below. A public inquest was held, and the jury returned verdicts of accidental death in accordance with the medical evidence.

This paper has been published for two reasons. The first is that accidents of this kind are extremely rare, and scientific observations even rarer—indeed, this is the first to be recorded in detail. The second is that a great deal of sceptical interest was shown in the opinion expressed at the inquest, after evidence of the autopsy findings, that death "could have occurred very quickly, perhaps within 30 seconds of being crushed." The factors causing sudden death in the early stages of asphyxial events are but little recognised. The circumstances are usually accidental or criminal in character and not therefore commonly experienced except in forensic medical practice. They certainly have no relation to everyday experience in holding one's breath, and relatively little to quiet physiological experiment.

AUTOPSY FINDINGS

CASE 1.—Girl aged 4 years. Extricated dead. Autopsy 42 hours after death. A healthy subject of good physique, 3 ft. in height. Marks of injury, which were not extensive externally, were in keeping with heavy progressive pinning and crushing, causing fatal asphyxia. The principal weight was borne by the l. shoulder and chest, and examination gave ample evidence that, at the time, the body was being bent in an acute bow backwards, in violent hyperextension (see below). Deep asphyxial discoloration of the skin was present in the head and neck, the entire r. arm, the extremity of the l. arm, and appreciably less in the lower trunk and legs. Clothing pressure marks were well-defined over the l. shoulder and chest and accompanied by a broad area of bruising over the l. front chest—some 3 in. by 2 in. Abrasions were present over the chin, ground downwards and to the r. for 1½ in., in keeping with a booted foot pressing and sliding. The neck had thus been bent backwards sufficiently to stretch and tear the prevertebral ligaments, and even more stretching was evident in the mid-trunk region, hæmatomata beginning to develop in the prevertebral tissues. Apart from slight surface bruising of the l. lung and faint bruising of the front wall of the l. ventricle—both from pinning and crushing of the chest—together with a local bruise to the l. side of the larynx 1 in. across, no other material injury was found. These sites of bruising were, however, regarded as vital situations, capable of far-reaching effects. No muscle changes were found.

CASE 2.—Boy aged 7 years. Extricated dead. Autopsy 60 hours after death. A healthy subject of good physique,

1. This and the other quotations are from the evidence of witnesses at the inquest.

4 ft. 1½ in. in height. There was intense cyanosis and congestion of the upper half of the trunk, the head and neck and both forearms and hands, the r. rather more than the l. Heavy pressure marks were present across the entire face, the front of the chest and the upper part of the abdomen. Glancing abrasions were present across the r. chin, to the l. thumb, to the first finger knuckle, and for 4 in. down the r. shin. Three small abrasions, one an inch and two ½ in. across, were present on the l. calf, and spot abrasions were present on both kneecaps. There were no marks on the back and no muscle crushings. Internal examination revealed intense asphyxial changes consequent on compression of the trunk, emptying under pressure of the stomach, and inhalation of vomit. Two small splits in the cardiac mucosa adjacent to the cardiac orifice gave evidence of increased intragastric pressure. The quantity of mixed vegetable food present had clearly not been excessive. No muscle changes were found.

CASE 3.—Girl aged 2½ years. Extricated dead. Autopsy 60 hours after death. A healthy subject of good physique 3 ft. 2 in. in height. This case, sister to case 2, showed very similar changes. There was similarly intense asphyxial congestion and cyanosis in the head and neck, across the shoulders, in both upper arms and wrists and hands, more marked on the l. than the r. These colour changes were relieved by heavy clothing pressure marks across the l. side of the trunk from the root of the neck to the hip region. There were more localised pressure marks with surface abrasions over the l. cheek, down the l. side of the mouth, and on the l. side of the chin. A further area of local bruising lay at the centre of the l. groin. None of these was heavy. Two spot bruises lay on the inner aspect of the r. thigh. Internal examination gave evidence of heavy compression of the chest and the abdomen, there being slight surface bruising of the heart muscle over the front wall of the l. ventricle, but no bruising of the lung. Asphyxial changes had followed the inhalation of vomit, which, as in case 2 had passed deep into the air-passages; it was not merely impacted at the glottis. No pressure splits were present in the stomach in this case, although it contained the same moderate quantity of food. No muscle changes were found.

CASE 4.—Boy aged 18 years. Extricated alive 2½ hr. after the start of the incident; admitted to the London Hospital about 5 min. later; died 3½ hr. after start of incident. Subjected to mass compression for 2–2½ hr. A healthy subject of very strong physique, 5 ft. 4 in. in height. Particularly heavy and sustaining pinning pressure was evident across the l. side of the trunk from shoulder to hip region, and even heavier pressure was evident across the l. thigh. Heavy clothing pressure marks extended from the l. mid-chest across the l. abdomen to the l. forearm, and reached down the l. upper leg. Intense asphyxial congestion with many petechial hæmorrhages had become developed over the scalp, head and neck, causing bleeding from the r. ear, and over the shoulders. Glancing abrasions were present over the back of the l. forearm and wrist, and sustained direct pressure abrasions were present on the l. brow and the r. upper and lower lips, the latter crushed and bleeding slightly. Evidence of the weight of pressure on the l. trunk was given principally by the stomach and intestines. These had already developed a traumatic paralytic dilatation. The stomach measured 10 in. by 5½ in. in its principal dimensions, though containing only some 2–3 oz. of fluid; the small intestines had become correspondingly dilated. No bony injuries were present. The grave asphyxial changes already manifest from external examination were even more pronounced in certain internal organs, petechial hæmorrhages being found in the lung, heart and voluntary muscle, fascia and brain. The ventricular fluids were tinged with blood from subependymal petechiæ of the same kind.

Remarkable ischæmic necroses of muscle were present in both thigh flexor groups. Affected muscle was a pale walnut-brown, swollen, over-moist but not watery, flecked with occasional muscular and fascial hæmorrhages, and merging with surrounding muscle through zones of incomplete necrosis which tended to confuse its precise outline. The conditions found were identical with the muscle necroses seen in war injuries, where the patient has been pinned down by beams and masonry, accompanied by myohæmoglobinæmia and myohæmoglobinuria, by urinary suppression and sometimes death, with renal changes as described by Bywaters and Dible (1942). The kidneys were retained together with portions of muscle and referred to Bywaters for examination, although it was felt that too little time had elapsed for renal changes to become established; no such changes were in fact seen.

DISCUSSION

The cause of death in these cases, although expressed generally as asphyxia due to suffocation by compression in a crowd, was clearly complex. Asphyxia is by no means one of the simple problems in medicine. The word itself, derived from the Greek a-sphuxis, means pulseless—not, as is popularly supposed, prevented from breathing. It seems likely that the Greeks were closer to the truth, for their word is pregnant with a meaning which our own adopted interpretation has lost. Emotional, reflex neurogenic, local cardiac and more general tissue chemical changes, direct compression of the chest or abdomen or constriction of the neck, concussional head-injuries and inhalation of vomit inhalation may all be operating in groups or together. Many of these are capable of precipitating death within a few seconds, yet except in forensic practice they often pass unrecognised. Cases 1, 2 and 3, extricated dead, showed changes quite out of keeping with prolonged asphyxia, and since the precise factors operating in each case cannot be detailed it may be more helpful to discuss the causation of death in criminal manual strangulation where closely parallel factors operate.

1. If the victim is frail and highly emotional she may die "of fright," from arrest of respiration and the heart beat, even before she is touched. Any forensic expert will have in his records a group of cases where death has occurred from the emotional disturbance of seeing approaching death—even of seeing danger or hearing bad news. A victim may die even of "anticipating asphyxia," and within a matter of seconds only, sufficient for a mere fluttering arrhythmia, then collapse and death.

2. If you select a vital part of the vagus sheath line—best of all if the thumb is placed on the carotid sinus—you may, the moment you exert pressure, induce a classical vasovagal inhibition, a carotid sinus reflex arrest of respiration and circulation. We are beginning to realise how commonly such a mode of death ensues during the preliminaries of an asphyxial event. Impaction of food at the glottis, or water in drowning, ju-jitsu garrotting or strangling, smart blows on the neck, even it is suggested a brisk current of cold air, are all likely to stimulate this or other receptive ends of this dangerous reflex. Gardner (1942) has recently discussed a group of such cases. Vomiting may result from asphyxia and merely constitute an incident in the course of such a death; this is likely to be forgotten in dealing with infant deaths. There may, on the contrary, be good evidence at autopsy that the inhalation of vomit has contributed materially to death, even where no asphyxial changes have developed. The impaction of food even in the smallest fragments (Moritz 1942) may precipitate death from reflex vagal inhibition, and death then follows so rapidly as to be virtually instantaneous. Case 1 showed a local bruise of the left side of the neck over the larynx and booted foot abrasions crushed down from the chin across the neck, the neck being violently hyperextended. Reflex vagal inhibition might well follow and cause death from these receptive injuries alone. Cases 2 and 3 had inhaled vomit, and although not classically impacted at the glottis this also was clearly capable of causing death without prolonged asphyxia; the absence of such changes form part of the basis for the view that death had taken place quickly. It should also be remembered that bending alone may cause regurgitation of food and initiate such an event.

3. Local biochemical changes in the heart muscle ensue with great rapidity in asphyxia, and their effects on its contractility and conductivity must be most significant in relation to death. At asphyxial arrest in situ, according to Chang (1938), "the rabbit's heart has lost 75% of its phosphagen, 90% of its glycogen, and 75% so its adenosine triphosphate." The fall in phosphagen if deeper than that in glycogen which is itself about twice as deep as the fall in pyrophosphate. In a minute the phosphagen may fall to a little over 60% of the initial value, and in two minutes as low as 30%. In the same period glycogen may fall to 80% and 60% of its initial value. It appears that phosphagen constitutes the immediate source of energy for the contraction of heart muscle. Asphyxia produced mechanical failure in about two minutes, "a significant impairment of myocardial

contraction appearing after 30 seconds to 1 minute of ischæmia." Asphyxia has also been shown by several workers to result in a rapid disappearance of the P-wave, ventricular automatism, and an electrocardiogram consisting of R-waves only.

4. More general changes in blood chemistry of material significance appear with alarming rapidity. "Asphyxial conditions raised the serum potassium from 12 mg. per cent. to 38 mg. in 4 to 5 minutes" (Patterson 1942). "The blood serum of these animals" (cats) "was subject to large and rapid variations of K under apparently physiological conditions" (Cattel and Civin 1938). An even more important result of oxygen starvation is seen in the brain and spinal-cord tissues, whose vulnerability to anoxia has been reviewed by Sugar and Gerard (1938) using the electroencephalogram. The time required for the disappearance of potentials after the beginning of generalised cerebral anoxia varied between 10 sec. and 2 min. according to whether subcortical white matter or medullary tissues were concerned. Putnam (1937) has suggested that this depends on an inherent difference in parenchymatous sensibility rather than on local differences in blood-supply—as might seem reasonable. According to van Harreveld (1939), there exists in the spinal cord of the cat a centre which depresses or inhibits its reflex excitability and which is less resistant to asphyxia than those involved in the excitatory part of reflex function. So the vulnerability to reflex inhibition increases with asphyxia. These general observations are likely to apply to case 4 in particular, but certainly contributed to the causation of death where any material degree of asphyxia developed.

5. If the victim is knelt on the pressure exerted on the intestines or their mesenteries may produce an arrest of respiratory rhythm and a fall in blood-pressure (Crowley 1942). Crushing pressure on the chest, especially if involving the heart—as was evident in cases 1 and 3, so much more likely in a young subject with an elastic compressible thoracic cage—may do precisely the same, or arrest both respiratory and circulatory rhythm (Moritz and Atkins 1938). Case 4 showed grave thoracic and abdominal crushing but survived to show equally serious secondary changes resulting from these injuries.

6. Where the head is beaten against some surface further ill effects may follow. After delays as short as 1–2 min. after a blow, embarrassment or failure of respiration may follow from contusional or postcontusional œdema of the bulbar centres (Denny-Brown and Russell 1941).

7. A similar effect may follow increasing—progressively stronger or heavier—compression of the neck. Extreme congestion in the head above this level may cause a shower of small hæmorrhages both in the skin and in the deeper tissues such as the brain substance or its membranes. These were noted in case 4. Their effects will be much the same as those developing from contusion. Pressure sufficient, and sufficiently accurately located, to occlude both carotid arteries and cause immediate and continued cerebral anæmia seems to be rare in forensic practice.

* * *

Danger to life clearly ensues within seconds of the start of events. It was not merely out of sympathy with the relatives or for political reasons that the opinion was expressed that death "could have occurred very quickly, perhaps within 30 seconds of being crushed." We should do well to remember the time factor in asphyxia when emotional, vagal, carotid sinus, chest and abdominal compression, inhaled vomit, biochemical and other less important factors are operating together. Only seconds are available to save life. This shelter disaster was no cool physiological experiment. Factors dangerous to life were being combined in groups throughout that mass of people and death picked out its victims here and there according to the mathematical whims of these factors. It was for this reason that "almost the last person removed from the bottom . . . stood up and walked to the first-aid post unaided."

This disaster provided a remarkable objective expression of the factors involved in the causation of death during asphyxial events. It also provides a solid basis for opinions on the time factor in criminal forensic practice.

SUMMARY

An account of the circumstances of the recent tube shelter disaster is set out, and the autopsy findings in four selected cases are described in detail.

The mode of death is discussed by reference to the causation of death in asphyxial events in general, more particularly as encountered in criminal deaths from asphyxia because it is felt that the rapidity with which a fatal result may ensue is little recognised. The factors which may contribute to rapid death are given a physiological basis and their forensic importance is stressed.

I am grateful to the coroner to the district concerned for access to the depositions at the inquest. For reasons of security all material names and times have been omitted as well as any controversial matter which might prejudice civil proceedings. I have had advice on physiological points from Mr. W. R. Spurrell and have discussed the forensic interpretations with Dr. Eric Biddle, Dr. F. E. Camps, Dr. Eric Gardner and Dr. R. D. Teare.

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GAS GANGRENE

ACTIVE IMMUNISATION BY MEANS OF CONCENTRATED TOXOIDS *

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THE three most important organisms causing gas gangrene are *Cl. œdematiens*, *Cl. welchii* and *Cl. septicum*, and the work here described involved the infection of guineapigs, separately, with each of them. The aim was to test the value of small doses of concentrated toxoids in immunising the animals against infection with organisms of the species corresponding to the toxoid.

Active immunisation with toxoids of various kinds has been under consideration for some time and the example most closely approximating to this study is the immunisation against tetanus practised in this country since the beginning of the war. This is now so well known that it need not be reconsidered.

Previous workers, including Kolmer (1941) Penfold & Tolhurst (1941) and Stewart (1942) have shown that some degree of immunisation can be obtained against gas-gangrene organisms and that the limiting factor is the production of a good toxoid. The work of Stewart on *Cl. welchii* is the most important of these studies and our results are in substantial agreement with her conclusions.

The toxoids used were prepared by Mr. B. C. J. G. Knight, D SC, Mr. W. E. van Heyningen, PH D, and Mr. D. Herbert, PH D, who have made available innocuous concentrated and partially purified antigens. They were in each case made from a single strain of high toxigenic capacity. The organisms used for the infections were derived from strains other than those used in making the toxoids, except in the case of *Cl. welchii* where the homologous organism was used together with another pathogenic strain. The animals received an initial dose, followed after an interval varying between 10 days and 3 weeks by a second dose; this constituted the primary immunisation.

The duration and value of this was explored in some of the animals. Others received a third dose after an interval of about 11 weeks. This additional dose, given at a period when the antitoxin content of the blood was found to have dropped considerably, caused a marked

* This work has been carried out on behalf of the Medical Research Council's subcommittee on anaerobic wound infections.
† In receipt of a grant from the Agricultural Research Council.

TABLE I—PROTECTION AGAINST *Cl. œdematiens* AND *Cl. welchii* INFECTIONS IN ACTIVELY IMMUNISED GUINEAPIGS

Organism	Expt.	Immunisation with toxoid				Infection		Survivors	
		Two primary doses		Secondary dose		Time after last dose	Level of attack	Immunised	Controls
		Total Lf	Interval	Interval	Lf				
Cl. œdematiens	1	20	3 wks.	..	..	8 wks.	1000–5000	4/5	..
							100– 500	6/6	..
Washed and heated spores with $CaCl_2$							10– 50	..	0/6
	2	30	3 wks.	..	..	20 wks.	100	7/7	1/5
Strains: Jolly, Domange	3	30	3 wks.	14 wks.	10	6 wks.	1000	7/7	0/5
Cl. welchii	4	40	3 wks.	..	..	12 days	1000–20,000	17/17	
							1– 2000		2/19
Washed vegetative bacilli with $CaCl_2$									
Strains: S107, SR12	5	25	3 wks.	..	..	8 wks.	20,000	2/6	0/6
							1000	6/7	0/5
							100	6/6	0/6

rise in the titre and inaugurated the secondary immunity which was also tested by exposure to infection.

It is appreciated that further study of the optimal amounts and the spacing of the immunising doses might further improve the results. Some measurements of the titres produced in the blood of the animals were made. The number of these estimations is small, and while they are of interest as indications of the corresponding titrés of circulating antibody found at various levels of resistance, there has been no attempt to make an exhaustive examination of this aspect of the response.

Measurements of circulating antitoxin were not made in the case of *Cl. œdematiens*.

The egg-turbidimetric method (van Heyningen 1941) was used for the majority of the estimations of *Cl. welchii* antitoxin. This method has its limitations with sera containing less than 1 unit per c.cm. owing to interference by the amount of serum protein present. Miss M. G. Macfarlane, PH D, therefore kindly obtained the lower values by the lecithinase method (Macfarlane & Knight 1941) which is not affected by the serum proteins. We are grateful to Dr. M. M. Barratt for determining the antitoxin titres in the case of *Cl. septicum*.

The immunising doses are expressed in Lf values.

METHODS OF INFECTION

The method of infection in the case of *Cl. œdematiens* and *Cl. septicum* was the intramuscular injection of 0·25 c.cm. of a washed and heated spore suspension in distilled water to which 0·25 c.cm. of 5% $CaCl_2$ solution had been added before inoculation. A sufficiently rich yield of spores of *Cl. septicum* was obtained by growing strain Pasteur III on Dorset egg medium (Henderson 1940) and the more difficult task of obtaining a rich suspension of spores of *Cl. œdematiens* was achieved by the use of a combination of coli-fermented broth with Dorset egg slopes (Bliss, Long & Smith 1941). The stock spore suspension was of the density of Brown no. 8 tube, and serial dilutions were prepared from it for each experiment.

With *Cl. welchii* a four-hour culture grown on serum-peptone water with beef juice and 0·45% glucose (Robertson & Keppie 1941) was washed in 1·0% peptone water and diluted to form a suspension of a known opacity (No. 5) measured by the Brown opacity tubes. This was diluted in a descending series in peptone water to twice the desired concentration. The sterile calcium chloride solution in distilled water was added immediately before intramuscular injection. These processes were carried out as rapidly as possible. A rapid technique with the minimum of delay between the interruption of growth and the inoculation of the bacteria is important if regular results are to be obtained. In all three cases animals were injected with a range of multiples of what was shown to be one certain killing dose from the titration within the experiment. This is a valuable analysis of the severity of the test and was carried out on every occasion.

While it is recognised that multiples of the lethal dose of living organisms may be an erroneous conception, it is important to push the numbers of organisms up as high as is reasonably possible to show the point at which resistance breaks down.

RESULTS

The results are set out in tables and in a selection of illustrative protocols chosen from the many different experiments made.

Cl. œdematiens.—The protection with *œdematiens* toxoid (experiments 1, 2 and 3, table I) appears to be extremely effective, the immunised animals surviving 100 to 5000 times the amount found to be one killing dose from parallel tests in unimmunised controls.

The protection shown in expts. 2 and 3, table I, was very good but did not reveal any difference between those with a primary immunity and those which had received a further stimulating dose. So an attempt was made to break down the resistance in the 14 animals which had withstood the infection in this test. They had shown no lesions and it seemed reasonable to suppose that the circulating antitoxin would not have increased in response to the aborted infection. These animals were therefore exposed 6 days later to a second infection with 10,000 times a lethal attack and they again resisted without lesions, while all the controls (8/8) died.

TABLE II—EFFECT OF A STIMULATING DOSE OF *Cl. welchii* TOXOID ON THE RESISTANCE TO ATTACK

Level of attack in killing doses	Survivors: immunised		Survivors: controls
	2 primary doses	Primary + secondary doses	
10,000–200,000	8/9 Moderate lesions. Gas gangrene arrested	10/10 No lesions	0/10
100–1000	9/10 Moderate lesions. Gas gangrene arrested	..	0/10
1–10	..	..	0/6

Infection: *Cl. welchii*, S107 washed vegetative bacilli.
Immunisation:
Primary: 2 doses total 30 Lf 3 weeks apart. Tested 20 weeks later: 0·2 antitoxin unit per c.cm. in blood.
Secondary: 10 Lf at 11 weeks. Tested 9 weeks later: 2·5–3·0 antitoxin units per c.cm. in blood.

This experiment also failed to discover any distinction between the resistance of those animals which had only two doses of antigen (expt. 2) and those which had had in addition a third dose after a long interval (expt. 3). It is remarkable that the animals had a solid resistance 5 months after the primary immunisation, but it should not be concluded that a third dose would not be useful in man. At suitable periods, the animals were bled in order that their serum might be examined for agglutinins. The results were negative, neither somatic nor flagellar agglutinins being demonstrated.

Cl. welchii.—The protection given by the *welchii* toxoid (expt. 4, table I) is also good but expt. 5 indicates that after a lapse of time the degree of protection against the highest levels of attack tends to decrease compared with animals tested at the height of the primary immunity. Further experiments on the value of a stimulating dose in increasing the resistance are shown in table II.

Though the investigation of the optimal antitoxin response in relation to the size and spacing of the doses of toxoid is outside the aim of this work, some indication of the correlation between the level of circulating antitoxin and the level of resistance to graded attacks was obtained.

Example A.—After a primary immunisation of three doses (total Lf 40) at three weeks' interval, the antitoxin titre (egg turbidimetric test) at 2, 4 and 11 weeks respectively after the third dose, was approximately 3·5, 2·0 and 1·5 units per c.cm.

At 11 weeks a stimulating dose of 10 Lf of toxoid was given which raised the titre to 8 units at 8 days, a level of 8 to 10 units being maintained for 4 weeks.

Example B.—After a primary immunisation of 30 Lf in two doses at three weeks' interval, the titres at 2, 4, 11 and 20 weeks respectively after the last dose were 3, 2 and 1 units per c.cm. (egg turbidimetric test) and 0·2 unit (lecithinase test). A stimulating dose of 10 Lf given at 11 weeks raised the titre to 7·0 units in 8 days, with a subsequent fall to 1–3 units in the succeeding 8 weeks. Twenty-three weeks after the stimulating dose, the titre of these animals was between 0·6 and 0·9 unit per c.cm.

After this degree of immunisation, an antitoxin titre of 0·2 unit/c.cm. circulating in the blood of a guineapig appears to correspond to a substantial degree of protection (table II) while with titres of about 2·5 to 3 units the animals were completely resistant to very high levels of attack. The data set out in this experiment (table II) were added to in a later test involving six animals which were immunised in this way with a stimulating dose at 11 weeks but were then retained for 23 weeks and exposed to 1000 times a lethal attack of living organisms. Five out of the six resisted completely without lesions of any kind being produced while one died of gas gangrene. Their titres as recorded above ranged about this time from 0·6 to 0·9 unit. These animals had been under experiment for 9 months and the one death is either a case of an animal failing to react as well as the others or is due to some contributory cause not revealed at the post-mortem examination. The enhancing effect on the antitoxin titre of a local infection in protected animals was examined. A group of animals was exposed to infection 8 weeks after a primary immunisation when their antitoxin titre was 1 to 2 units per c.cm. and the survivors had local lesions of varying degree which regressed.

The titres of the resisting animals were: at 3 days after infection, 1 to 2 units; at 5 days, 1 to 2 units; at 13 days, 2 to 5 units. The rise in titre at 13 days is significant but there is a lag of at least 5 days in the antitoxin response to the stimulus of the infection.

The effect of a stimulating dose on the titres of animals which had been given a primary immunity by the injection of *Cl. welchii* toxoid was also observed in 8 rabbits. This injection after 11 to 14 weeks produced a considerable increase in the titre above the moderate primary response but the rise did not begin in any case till the 3rd day and was not very substantial until the 5th day.

Cl. septicum.—The conditions for protection with *septicum* toxoid seemed to differ somewhat from those observed with *œdematiens* and *welchii*. In the preliminary experiments carried out with doses comparable in terms of Lf content of antigen with those used successfully with the other toxoids,‡ no resistance whatsoever was shown against 10 times a lethal attack (expt. 1, table III).

The Lf of the toxoid dose for a satisfactory primary resistance (expt. 2) was found to be 150 Lf given in two doses 3 weeks apart. Animals immunised in this way and kept for 11 weeks had titres of less than 1 unit per c.cm. and showed a considerably decreased resistance to infection (expt. 3a). If a stimulating dose (50 Lf) was given at 10 weeks after the primary immunisation, the titre at the peak of the response (10 days) was 3 units and the animals were solidly resistant to 1000–5000 times a certain killing dose of live spores (expt. 3b, table III). This shows that in spite of the invasive character of *Cl. septicum* an animal can be protected against a very high level of attack on what must be primarily and probably entirely an antitoxic basis.

Expt. 4, table III, shows the result of a test 9 weeks after the stimulating dose. The antitoxin titre of the pooled sera was about 1 unit/per c.cm. There were only 8 animals available and they were exposed to the same high level of attack (1000–5000 killing doses) as that used in 3a and 3b. It will be seen that 5 out of 8 were completely protected; this is in sharp contrast with the result in 3a, where at a comparable interval after the last dose of toxoid in a primary immunisation the animals all succumbed to this attack.

It should be observed that while the value of the protection in the stimulated animals has declined when compared with the test of this group at 10 days, which is the peak of the secondary immunity, the degree of resistance is still very substantial against what must be considered a very severe test.

The falling-off in the resistance with time has not been so well explored because of practical considerations and we would point out that while the theoretical basis seems clearly established the dosage and the assessment of the adequate level of antitoxin necessary for continued protection should probably be based on a higher circulating titre than that suggested in these experiments.

As was the case with *œdematiens* toxoid, agglutination tests for bacterial antibodies were again negative when the sera from the animals immunised with *septicum* toxoid were examined.

DISCUSSION AND CONCLUSIONS

The toxoids used for immunisation in these experiments were in all cases derived from the supernatant fluid of cultures, the bacteria being discarded. They are toxoids in the strict sense of the word. In *Cl. welchii*, for example, it is the alpha (lethal) toxin that is titrated and while other elements may no doubt be present this is primarily an α antitoxin immunisation. Any soluble antibacterial elements present must be minimal in quantity and can exercise very little, if any, effect. This is borne out by the experimental finding that the sera from animals immunised with *Cl. œdematiens* and *Cl. septicum* toxoid contained no agglutinins for the homologous organisms. In all three cases this is an antitoxic immunisation. The mechanism is readily explicable in these species because the proliferation of the organisms beyond the necrotic area of the inoculation depends upon the damage done to the tissues by the toxin and on the paralysis of the leucocytic action which it sets up.

It has been shown here in *Cl. welchii* and *septicum*—and it applies no doubt to *œdematiens* also—that this type of protection depends on an adequate amount of antitoxin circulating in the blood and only so long as it is

‡ It should be noted that the Lf value of different antigens is referred to the international units of the corresponding antitoxin, which are entirely distinct one from the other; a numerical difference in Lf content does not necessarily mean that the content of antigen protein is different.

TABLE III—ACTIVE IMMUNISATION AGAINST *Cl. septicum*

Organism	Expt.	Immunisation with toxoid				Infection		Antitoxin in blood of animals units /c.cm.	Survivors	
		Two primary doses		Secondary dose		Time after last dose	Level of attack in killingdoses		Immunised	Controls
		Total Lf	Interval	Interval	Lf					
Cl. septicum	1	40	11 days	..	..	24 days	10	..	0/6	0/4
	2	150	3 wks.	..	..	2 wks.	1000	2·0	4/5	0/5
		150	3 wks.	..	..	2 wks.	100	2·0	5/5	0/5
Washed and heated spores with $CaCl_2$ Strain: Pasteur III	3a	150	3 wks.	..	..	11 wks.	1000–5000	< 1·0	0/6	0·8
							100	< 1·0	3/4	0/5
	3b	150	3 wks.	10 wks.	50	10 days	1000–5000	3·0	8/8	0/8
	4	150	3 wks.	10 wks.	50	9 wks.	1000–5000	< 1·0–>1·0	5/8	0/8

present is the animal protected. If this condition is achieved, very massive attacks by the living organisms are resisted.

It is important that this should be realised. It is also clear that the enhancing effect on the titre of a primarily immunised animal, whose immune-body capacity has been trained, does not come into play—whether the antigen is presented as toxin in the course of an infection or as a further dose of toxoid—for a period of between 3 and 10 days. This time-lag must be borne in mind in applying these data to man; owing to the rapid onset of gas gangrene, the essential condition for protection is that antitoxin should already be circulating in the blood at the time of exposure to infection.

SUMMARY

Small doses of toxoid protected guineapigs against the three organisms most frequently causing gas gangrene—*Cl. welchii*, *Cl. œdematiens* and *Cl. septicum*. Protection depends on the presence of an adequate amount of antitoxin in the circulating blood of the animal.

In addition to the acknowledgements already made, we would like to thank Mr. J. S. Paterson, MRCVS, PH D, of the Institute of Animal Pathology, Cambridge, for valuable help in providing the animals and supervising the care of them.

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FACTORS AFFECTING THE RESPONSE OF IMMUNISED GUINEAPIGS TO ANTIGENIC STIMULUS

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WHEN a dose of specific antigen is given to an animal which has been actively immunised many months or even years before, and in which the circulating antibody has declined to a low level or may be no longer detectable, there is almost always a rise in the antibody content of the blood. After a delay of 3–5 days the antibody begins to increase, and it reaches a maximum concentration about 10 days after the reinjection of antigen.

The object of our experiments was to see whether this customary response to antigenic stimulus occurred when the animals were kept under adverse and abnormal conditions, including restriction of diet, exposure to cold, and non-specific infection.

About 100 guineapigs, all bred at the Medical Research Council's farm laboratories, were available. They had been used for studying the immunity produced by the diphtheria prophylactic alum-precipitated toxoid (APT). Each had received an injection of APT equivalent to 1 flocculation unit, and 4 weeks later a second injection of the same amount. The antitoxin content of the serum was determined 10 days after the second injection and again four times at intervals of about a month, the last sample being taken 8 months after the first injection of antigen. The rate of decline of antitoxin in the circulation was thus determined for each animal, and with few exceptions it followed the normal course: the decline was rapid during the first month after the first bleeding; it was small during the next month; and there was little change during the rest of the eight-month period.

All the guineapigs used in these experiments had behaved in this general way, although the maximum antitoxin level recorded 10 days after the second injection, and the level maintained in the later months, was higher in some than in other.

During these eight months the animals remained well. At the beginning of the immunisation they weighed from 280 to 350 grammes, and their weight increased to 500–600 g. or more; apart from occasional fatalities following heart puncture there were no deaths among them.

EXPERIMENT I

A group of 42 animals was divided into four smaller groups (10, 10, 10 and 12) in such a way that each group contained some with a relatively large, some with an intermediate, and some with a relatively small amount of circulating antitoxin. For eight months they had lived under the same favourable conditions.

They were housed in the same room, which was light, airy, well ventilated and panel-heated, in cages made entirely of metal. These consisted of a shallow tray-like base, 15 × 20 in., and a cover made of wire 12 in. high which fitted loosely into the tray. Each cage accommodated 4, and occasionally 5 animals, those in one cage always being of the same sex. Sawdust was used for litter and hay was supplied daily. In the morning each animal was given a daily ration of bran (15 g.) and sugar-beet pulp residue (15 g.) made into a mash with water, and about 50 g. of cabbage per guineapig per day was given as the evening feed.

For the purposes of the experiment the four groups were treated as follows:

(*a*) *Controls.*—For 10 guineapigs the living conditions remained as before.

(*b*) *Restricted diet.*—10 were given water, but deprived of food for 48 hours. They were then given the same daily ration of bran and sugar-beet pulp as the control group for an additional 3 days before the injection of antigen, and this diet was continued for the remaining 10 days of the experiment. They were not given hay or cabbage.

(*c*) *Exposure to cold.*—10 were transferred in their cages between 9 and 10 AM to a room with a temperature constantly at − 2° C. to − 4° C., and remained there until 4–5 PM. They were then transferred, in their cages, to the roof of the institute and remained there, in the open, until 9–10 AM next day, when they were taken back to the cold room. This procedure was repeated daily for 3 days before the injection of antigen and during the remaining 10 days of the experiment. The animals of this group received the same diet as the control group. The experiment was carried out in the second half of October, 1942.

(*d*) *Welchii infection.*—12 were injected with a washed culture of *Cl. welchii* type A in the presence of calcium chloride. Contrary to expectation, based on earlier tests, only 2 survived for 10 days. This part of experiment I was accordingly repeated (expts. II and III below). The animals in this group, and those used in the two later experiments, were housed and fed like the controls.

Each animal was injected subcutaneously with the equivalent of 1 flocculation unit of APT, in 1 c.cm. of normal salt solution. At the time this injection was given the animals in group (*b*) had been kept without food for 2 days and on the restricted diet for 3 more days; those in group (*c*) had been exposed as described above for three days, and in those of group (*d*) infection with *Cl. welchii* was well-established after their injection 24 hours before.

The results are summarised in table I. It will be seen that all the surviving animals in all the groups showed an increase in antitoxin content, and it is clear that neither restriction of diet nor exposure to cold had a significant effect on this response.

One point with regard to the design of the experiment, and one with regard to its execution, may be mentioned briefly here.

So that the effects of adversity could be evaluated the dose of antigen had to be such that, in the control group at least, the response should not be maximal, and yet at the same time it must be measurable. That the dose injected was not too small is evident from the fact that in every animal the antitoxin concentration after 10 days was at least twice its original value. That it was not too large is clear because in similar experiments with animals at the same stage of immunisation, a larger dose of antigen was followed by much larger increases in antitoxin concentration. In one such experiment the antitoxin content of pooled serum from 50 similar guineapigs was 40 units per c.cm. That the dose of antigen injected was submaximal is also suggested by the fact that when the original antitoxin was high the increase was relatively small and when the original titre was low the increase was relatively large.

TABLE I—INCREASE OF CIRCULATING ANTITOXIN ON INJECTING ANTIGEN INTO IMMUNISED GUINEAPIGS: (*a*) KEPT UNDER NORMAL CONDITIONS, (*b*) GIVEN A RESTRICTED DIET, (*c*) EXPOSED TO COLD, (*d*) INFECTED WITH *Cl. welchii*, TYPE A

(*a*) Normal controls			(*b*) Restricted diet			(*c*) Exposed to cold			(*d*) *Cl. welchii* infection		
AT units/c.cm.		Increase in AT	AT units/c.cm.		Increase in AT	AT units/c.cm.		Increase in AT	AT units/c.cm.		Increase in AT
Before antigen	10 days after		Before antigen	10 days after		Before antigen	10 days after		Before antigen	10 days after	
1	(1) 2	2 ×	2	(2) 4	2 ×	2	(2) 8	4 ×	0·125	0·25	2 ×
1	(1) 4	4 ×	1	(1) 4	4 ×	0·5	(0·5) 2	4 ×	0·125	4	32 ×
1	(1) 8	8 ×	1	(1) 8	8 ×	0·5	(0·5) 2	4 ×	..	..	..
0·5	(0·5) 8	16 ×	1	(1) 8	8 ×	0·5	(0·5) 2	4 ×	(10 died within 10 days)		
0·25	(0·5) 2	8 ×	0·5	(1) 2	4 ×	0·5	(1) 4	8 ×			
0·25	(0·125) 4	16 ×	0·5	(0·5) 4	8 ×	0·5	(0·25) 4	8 ×	..	..	..
0·25	(0·5) 4	16 ×	0·5	(0·5) 4	8 ×	0·5	(0·5) 8	16 ×	..	..	..
0·25	(1) 4	16 ×	0·25	(0·5) 8	32 ×	0·5	(0·5) 8	16 ×	..	..	..
0·25	(1) 8	32 ×	0·25	(0·5) 8	32 ×	0·25	(0·5) 4	16 ×	..	..	..
0·125	(0·125) 4	32 ×	0·25	(0·25) 8	32 ×	0·125	(0·125) 1	8 ×	..	..	..
Geom. mean 0·38	(0·5) 4·29	..	0·57	(0·7) 5·28	..	0·47	(0·5) 3·48	..	..	..	..

The figures in parentheses indicate antitoxin concentration on *fifth* day after injection of antigen.

For the execution of the experiment, the conditions had to be such that the guineapigs, or the great majority of them, should survive for 10 days. These conditions were achieved for those on a restricted diet and those exposed to cold, but not in group (*d*) (non-specific infection) in which only 2 out of 12 animals survived till the 10th day after the injection of antigen. It is to be noted, however, that these 2 which just survived 10 days despite typical signs of gas-gangrene, had an increase in antitoxin concentration.

The antitoxin content of the serum of 30 guineapigs was determined on the *fifth* day, as well as on the tenth day, after the injection of antigen. It will be seen (table I) that by the fifth day it had increased in 9, remained unchanged in 19 and decreased in 2. The beginning of the increase does not seem to have been retarded by restriction of diet and only very slightly by cold.

EXPERIMENT II

A small dose of a less virulent culture of *Cl. welchii* type A was injected into 15 of the guineapigs which had been immunised with APT.

The infection was induced by the method described by Armstrong and Rae[1] and used in this laboratory by Evans.[2] After 24 hours they all showed a large plum-coloured swelling at the site of inoculation (the muscles of the left thigh). Each of the 15 animals and 11 others which formed a control group was then injected with the equivalent of 1 flocculation unit of APT, all these injections being given subcutaneously on the right side of the middle line and upwards towards the right axilla. In all 15 animals of the infected group the disease progressed; typical gangrene of the thigh muscles developed during the second day, the tissues at the site of inoculation broke down, an open wound was produced, and the œdema increased until it reached the level of the diaphragm. In all cases there was extensive tissue damage and 3 animals died before the 10th day. Ten days after the injection of antigen the antitoxin titre of each of the 12 surviving animals of the experimental group and each of the 11 controls was determined. The 12 surviving animals in the infected group were then killed; they all showed extensive lesions typical of *Cl. welchii* infection, the organism being recovered in all cases from the thigh muscles and in 3 from the heart blood.

Table II shows that while the antitoxin response in the experimental group was slightly less than in the control group, all the animals—despite severe illness during the 10 days following injection of the antigen—showed an increase in antitoxin concentration.

1. Armstrong, A. R. and Rae, M. V. *Canad. med. Ass. J.* 1941, **45**, 116.
2. Evans, D. G. *Brit. J. exp. Path.* 1943. In the press.

EXPERIMENT III

This was carried out in a slightly different way.

A group of 21 animals immunised against diphtheria had been used for testing the protective action of *Cl. welchii* antiserum against a living virulent culture of that organism, the infection being induced as described above. The antiserum had been given three hours before the culture. Four days later it was clear that about half these animals had been fully protected by the antiserum and would almost certainly survive, while the other half exhibited symptoms of gangrene in varying degree.

At this stage all 21 animals were bled and each was given the equivalent of 1 flocculation unit of APT. Ten days later each of the survivors was bled again. All the animals were then killed, and cultures were made from the heart blood and from the muscles at the site of injection. On purely clinical appearances they were divided into two groups—(i) those with signs of gas gangrene, and (ii) those without. Excluding one animal which died during the 10 days of the experiment, *Cl. welchii* was cultivated from the thigh muscles of all the

TABLE II—INCREASE OF CIRCULATING ANTITOXIN ON INJECTING ANTIGEN INTO IMMUNISED GUINEAPIGS: (1) KEPT UNDER NORMAL CONDITIONS; (2) INFECTED WITH *Cl. welchii* TYPE A

(1) Normal controls			(2) Infected with *Cl. welchii*		
AT units/c.cm.		Increase in AT	AT units/c.cm.		Increase in AT
Before antigen	10 days after		Before antigen	10 days after	
0·5	4	8 ×	0·5	2	4 ×
0·5	8	16 ×	0·5	4	8 ×
0·25	4	16 ×	0·25	4	16 ×
0·25	8	32 ×	0·25	4	16 ×
0·25	8	32 ×	0·25	4	16 ×
0·125	4	32 ×	0·125	4	32 ×
0·125	4	32 ×	0·125	4	32 ×
0·125	4	32 ×	0·05	0·5	10 ×
0·125	8	64 ×	0·05	0·5	10 ×
0·125	8	64 ×	0·05	4	80 ×
0·005	4	800 ×	0·01	4	400 ×
			0·002	4	2000 ×
Geom. mean 0·15	5·48	..	0·09	2·67	..

animals with clinical gangrene (and from the heart blood of one of them) but not from any of the others.

The results in table III agree with those of expt. II. Again the response was slightly less in the infected group, but all except one of the animals showed an increase in antitoxin concentration in spite of an active infection involving considerable tissue damage. It is to be noted that in this experiment the infection had been established for four days before the antigen was given.

TABLE III—INCREASE OF CIRCULATING ANTITOXIN ON INJECTION OF ANTIGEN INTO IMMUNISED GUINEAPIGS: (1) WITHOUT GAS GANGRENE; (2) WITH GAS GANGRENE

(All had been infected with *Cl. welchii*, but group 1 had been protected with antiserum)

(1) No gas gangrene			(2) Developed gas gangrene		
AT units/c.cm.		Increase in AT	AT units/c.cm.		Increase in AT
Before antigen	10 days after		Before antigen	10 days after	
2	8	4 ×	1	2	2 ×
1	2	2 ×	0·5	1	2 ×
1	8	8 ×	0·5	2	4 ×
0·5	2	4 ×	0·5	8	16 ×
0·25	1	4 ×	0·25	0·25	0
0·25	1	4 ×	0·25	0·5	2 ×
0·25	4	16 ×	0·25	1	4 ×
0·125	4	32 ×	0·25	4	16 ×
0·05	1	20 ×	0·125	0·25	2 ×
			0·125	0·5	4 ×
			0·125	4	32 ×
Geom. mean 0·36	2·52	..	0·28	1·21	..

DISCUSSION

It may be argued that the conditions of these experiments were not so severe as they might have been made; but they were at least very different from those to which the animals had been accustomed, and they resembled to some extent those which healthy young adults might experience at the present time. Viewed in retrospect, the results suggest that the exposure to cold might have been longer and perhaps more severe, and that the diet might have been even more restricted, so that the physical condition of the animals would have deteriorated more before the antigen was injected. It is not possible to say whether guineapigs in an extremely emaciated and debilitated state would respond to antigenic stimulus, but the results obtained with those infected with *Cl. welchii* are suggestive; for these animals experienced such adverse conditions as only just permitted survival for 10 days after infection. The choice of this organism was fortunate because it established disease very quickly and this progressed during the 10 days of the experiment. Many of the animals which survived for this time were almost moribund when the final blood sample was taken; all of them had suffered a severe and protracted illness, with large wounds involving extensive tissue damage, during the whole time that the established immunising mechanism was being stimulated; and it is remarkable that the mechanism responded—only slightly less than in the normal healthy controls—in 22 out of 23 animals infected.

As it appeared possible that the results of these experiments might have some bearing on the procedures adopted for the prevention of tetanus in wounded or injured persons, the attempt was made to reproduce conditions somewhat resembling those in which human beings might require tetanus prophylaxis. These procedures vary in different armies, and opinion is still divided as to whether an immunised person who becomes a casualty should be given an injection of toxoid or one of tetanus antitoxin. Active immunisation against tetanus is compulsory in the armed forces of the United States and France, and the American and French authorities argue that, as the immunised casualty may have either an adequate concentration of circulating antitoxin or an established immunising mechanism which can be stimulated into activity either by exposure to natural infection or by the injection of tetanus toxoid, the administration of antitoxin is unnecessary.

The practice of giving toxoid, rather than antitoxin, has been questioned on several grounds. One is that there is a delay of some days before the circulating antitoxin increases; another is that, whereas an increase in antitoxin may be confidently expected to occur under normal conditions, it might be absent or greatly delayed in seriously injured persons, possibly with heavily infected wounds, suffering from shock, or otherwise affected by abnormal adverse conditions. In our experiments the adverse conditions to which the immunised guineapigs were exposed had little or no effect on their response to antigenic stimulus.

SUMMARY

The increase of circulating antitoxin which follows injection of an antigen (diphtheria APT) into immunised guineapigs was but little affected by exposure to cold, restriction of diet, or infection with *Cl. welchii*.

So far as they are applicable, these experiments suggest that, despite the adverse conditions of the battlefield and lowering effect of wounds, injured persons who have previously been immunised against tetanus or other infections may be expected to develop antitoxin in response to an antigenic stimulus.

PERSISTENCE OF TETANUS ANTITOXIN IN MAN FOLLOWING ACTIVE IMMUNISATION

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THE persistence of antitoxin for long periods after immunisation with tetanus toxoid under different conditions has already been demonstrated (Ramon and Zoeller 1933, Sneath and Kerslake 1935, Bigler and Werner 1941, Peshkin 1941). In this paper a comparison has been made between the persistence of antitoxin in immunised persons who receive a stimulating dose and those who do not.

In July, 1940, a number of the staff of the National Institute for Medical Research, Hampstead, received

TABLE I—TETANUS ANTITOXIN TITRES OF SERA FROM PERSONS RECEIVING TWO DOSES OF TETANUS TOXOID

Antitoxin titre (IU per c.cm.)

Before 1st inoculation	9 weeks after 1st inoculation	After 2nd inoculation	
		4 mos.	28 mos.
< 0·01	< 0·01	0·1–1	0·1–1
< 0·01	< 0·01	0·1–1	0·1–1
< 0·01	0·02–0·1	0·1–1	0·1–1
< 0·01	< 0·01	0·1–1	0·1–1
< 0·01	0·02–0·1	0·1–1	0·02–0·1
< 0·01	—	0·1–1	0·02–0·1
< 0·01	0·01–0·02	0·1–1	0·02–0·1
< 0·01	< 0·01	0·02–0·1	0·01–0·02
< 0·01	0·01–0·02	1–2	0·1–1
< 0·01	0·02–0·1	0·1–1	0·02–0·1
< 0·01	< 0·01	0·02–0·1	0·02–0·1
< 0·01	< 0·01	0·1–1	0·02–0·1
< 0·01	< 0·01	0·1–1	0·02–0·1
< 0·01	0·1–1	1–2	0·1–1
< 0·01	0·01–0·02	0·1–1	0·1–1
< 0·01	0·1–1	0·1–1	0·1–1
Geom. mean: < 0·01	0·02	0·11	0·04

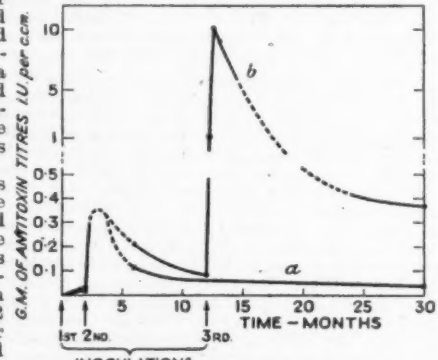
TABLE II—TETANUS ANTITOXIN TITRES OF SERA FROM PERSONS RECEIVING A THIRD DOSE

Antitoxin titre (IU per c.cm.)

Before 1st inoculation	9 weeks after 1st inoculation	After 2nd inoculation		After 3rd inoculation			
		4 mos.	10 mos.	5 days	12 days	30 days	18 mos.
< 0·01	< 0·01	0·02–0·1	0·02–0·1	0·02–0·1	2–5	2–5	0·1–1
< 0·01	0·02–0·1	0·1–1	0·1–1	2–5	10–20	10–20	0·1–1
< 0·01	< 0·01	0·02–0·1	0·02–0·1	0·1–1	2–5	2–5	0·1–1
< 0·01	0·1–1	1–2	0·1–1	2–5	20–50	20–50	1–2
< 0·01	0·1–1	1–2	0·1–1	2–5	20–50	20–50	1–2
< 0·01	—	1–2	0·1–1	5–10	20–50	20–50	1–2
< 0·01	0·02–0·1	1–2	0·1–1	2–5	20–50	20–50	2–5
< 0·01	0·02–0·1	0·1–1	0·1–1	1–2	10–20	5–10	0·1–1
< 0·01	0·1–1	0·1–1	0·1–1	5–10	20–50	20–50	0·1–1
< 0·01	—	0·1–1	0·1–1	2–5	10–20	5–10	1–2
< 0·01	0·02–0·1	1–2	0·1–1	2–5	10–20	10–20	1–2
GM = < 0·01	0·03	0·21	0·08	1·1	10·1	9·0	0·37

GM = Geometric mean.

two doses of tetanus toxoid, each of 1 c.cm., given at an interval of 9 weeks. The content of circulating antitoxin in the sera was determined before and after the first injection and also 4 and 10 months after the second. The effect of a third injection of toxoid, given 10 months after the second, was also investigated in 16 persons. The two first injections produced, in all the subjects, a concentration of antitoxin of more than 0·01 international unit per c.cm. and the third dose resulted in a large and rapid increase (Evans 1941).



Antitoxin titres in the blood of persons receiving (*a*) two doses, and (*b*) a third dose.

It was not to be expected that the high levels of antitoxin found 12 days after the third inoculation would be maintained for any considerable time. Indeed, in some of the 16 persons it was found that 30 days after the injection the concentration had already begun to fall. The advantages of a third injection of toxoid cannot therefore be judged merely by the immediate response.

It has now been possible, 30 months after the first dose of toxoid was given, to compare the antitoxin content of the sera of (*a*) those who received only two doses of toxoid and (*b*) those who received the additional dose.

Sera were obtained from 16 persons who had had two doses of toxoid and from 11 who had had three. Tables I and II give the antitoxin content for all these subjects before and after immunisation. The geometric mean for each series, calculated from the lower levels of the antitoxin titres, is also given, and these values have been used to represent the results graphically (see figure).

All the sera from the 16 persons receiving only two doses had less than 1 unit of antitoxin per c.cm. ; though none had less than 0·01 unit, half had less than 0·1 unit. Comparing these values with those obtained four months after the second injection, the antitoxin content was unchanged in 7 of the cases but somewhat reduced in 9.

All the sera from the 11 persons receiving an additional dose had more than 0·1 unit, and 6 of them had more than 1 unit. In no case was the antitoxin content of the persons in this group lower than the value obtained 4 months after the second injection ; in fact in 4 of the subjects it was even higher.

CONCLUSION

Administration of a third dose of tetanus toxoid increases the concentration of antitoxin in the blood. For 18 months at least, the concentration remains much higher than that resulting from two doses of toxoid.

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TANRET REACTION IN SUBTERTIAN MALARIA

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THE simple Tanret test for quinine in urine, as described in textbooks on tropical medicine, has been widely used to control the administration and absorption of quinine during the treatment of malaria. From observations on European troops in a hyperendemic area of subtertian malaria (Southern Nigeria) we believe that, properly used, the test has an even greater value than has been generally realised, but that mistaken ideas regarding its interpretation need to be removed.

Properly used the test may explain many apparent cases of "quinine resistance." Its use has suggested to us that abnormalities of quinine metabolism may play an important part in bringing about the state of "continued infection" which is recognised as favouring the onset of blackwater fever.

METHODS

We used the technique of the Tanret test described by Manson-Bahr (1940) and confirmed with our own reagent that it gives a positive reaction when quinine is present even in a dilution of 1:200,000.

Reagent.—Two solutions are prepared :—

Solution 1.—Mercuric chloride, 27 g., is dissolved by stirring in 1500 c.cm. of boiling distilled water.

Solution 2.—Potassium iodide, 100 g. is dissolved in 500 c.cm. of cold distilled water.

To prepare the reagent, which keeps indefinitely, mix solutions 1 and 2 and add 25 g. of glacial acetic acid.

Technique of test.—The urine must be cold and clear or false negatives will be recorded. Turbidity due to phosphates may be cleared with a few drops of dilute acetic acid : other turbidities may be removed by filtration. To about 10 c.cm. of urine add a few drops of reagent. If quinine is present in concentrations of 1 in 200,000 or more, turbidity will appear which disappears on heating. If turbidity persists on heating albumin is present. It is then necessary to take a second 10 c.cm. of urine and remove the albumin by precipitation with heat and acetic acid followed by filtration. The albumin-free filtrate should then be cooled and tested with the Tanret reagent for quinine.

Positive reactions are also found in the urines of patients taking plasmoquine but not of those taking other alkaloids in ordinary therapeutic doses.

We applied the test to every specimen of urine passed by 100 consecutive men admitted to hospital with subtertian malaria both during their acute attacks and in convalescence.

Treatment consisted of a week's course of quinine bisulphate in solution, given in three doses of grains 10 daily by mouth (a total of gr. 210 in a week). We never used tablets and took special precautions to prevent evasion of the drug, especially when negative Tanret reactions were found. When that happened, one of us saw the dose taken and made the man speak for a few moments to be sure that he swallowed it. When necessary, we saw urine passed. In no instance did our precautions alter the picture. After the week on gr. 30 a day, the dose was reduced to gr. 10 daily for 3 or 4

days, and then to gr. 5 daily before discharge. Tanret reactions were continued during this period. British troops in the area were under orders to take a daily dose of gr. 5 of quinine on parade as a suppressive of malaria, and it was common practice to increase the dose to gr. 10 for a short period after unusual stress or after an attack of malaria: hence the importance of the reactions during convalescence.

Controls.—53 soldiers in good health were given gr. 5 of quinine in solution by mouth and their urines were examined for Tanret reactions at intervals of 15, 30 and 60 min. after the test dose and then at hourly intervals until a positive reaction was found. A final specimen was examined from each man 24 hours after the test dose.

RESULTS IN ACUTE ATTACKS

Of the 100 soldiers, 88 showed a positive Tanret reaction within 2–3 hours of their first dose of quinine and continued to have strong reactions in all urines passed during their 7 days on gr. 30 a day. All these men became apyrexial in 72 hours at most and recovered uneventfully.

Of the other 12 cases, 7 showed negative reactions in all urines until a dose of intravenous quinine was given. While the Tanret reactions remained negative they were all acutely ill: after the intravenous quinine the Tanret reaction became positive and remained so, even when the same doses of quinine were again given by mouth. Recovery following the intravenous quinine was rapid. The remaining 5 showed occasional positive reactions at irregular intervals. They were not dangerously ill and were not given intravenous quinine but recovery was slow; pyrexia lasted 5 or 6 days and the Tanret reactions during convalescence were unsatisfactory.

Short records of these 12 men are given.

ALL TANRET REACTIONS NEGATIVE

CASE 1.—Aged 37. In West Africa 3/12 year. First attack. Admitted 2nd day of illness. Temperature 104·4° F. Diagnosis on clinical grounds. No vomiting. After gr. 30 of quinine in 24 hours Tanret negative in all urines. T. 103·6° F. Delirious. Quinine, gr. 10, intravenously. T. 98·4° F. in 12 hours. Tanret positive. Progress satisfactory.

CASE 2.—Aged 33. In WA 10/12 year. Admitted 1st day of 8th attack. T. 102° F. Malaria parasites (MT rings) +. In 28 hours quinine, gr. 40, by mouth. No vomiting. Tanret negative. T. 99° F., but very drowsy. Headache severe. MT rings ++. Quinine, gr. 10, intravenously. Tanret positive in 2–3 hours. Recovered. He developed blackwater fever 7 months later. Recovered.

CASE 3.—Aged 39. In WA 12 years. Uncountable previous attacks. Admitted 1st day. T. 102·8° F. Very ill. Complication—acute gonorrhœa. MT rings +. In 3½ days, quinine, gr. 100, by mouth. T. 100° F. Sharply ill. Tanret negative in all urines. No vomiting. Quinine, gr. 10, intravenously. Tanret positive. T. 99° F. for next 3 days and then normal. Good progress.

CASE 4.—Aged 29. In WA 1 3/12 years. Admitted 4th day of 2nd attack. Vomiting before admission. Quinine given before admission: amount unknown. Diagnosis on clinical grounds. T. 101·6° F. Fairly ill. Jaundice developed 3 days after admission, accompanied by vomiting. Tanret reactions negative after gr. 90 of quinine by mouth in 3 days. T. 101° F. Quinine, gr. 10, intravenously. T. 98·4° F. in 6 hours and Tanret positive. Improved. Though jaundice continued (icterus index 80) and nausea persisted, Tanret reactions now remained positive on oral quinine. No further signs or symptoms of malaria. Slow improvement of jaundice.

CASE 5.—Aged 32. In WA 1 7/12 years. Admitted 3rd day of 9th attack. T. 104° F. MT rings ++. Acutely ill. In 2½ days before admission gr. 70 of quinine given by mouth. Tanret reactions negative. No vomiting. Quinine, gr. 10, intravenously. Marked improvement. Tanret positive. Recovered quickly. Six months later developed blackwater fever with anuria: died.

CASE 6.—Aged 40. In WA 8/12 year; 7th attack; admitted 3rd day of illness. Quinine, gr. 70, orally before admission. Tanret reactions negative. Delirious. T. 103° F. No vomiting or other gastro-intestinal symptoms. Parasites not demonstrated, but clinical picture typical of malaria. Quinine, gr. 10, intravenously. T. 98·4° F. in 8 hours. Tanret positive: remained positive on oral quinine. Recovery uneventful.

CASE 7.—Aged 22. In WA 1 9/12 years; 7th attack. Admitted 1st day of illness. MT rings +. T. 101° F. Very drowsy. After quinine, gr. 40, by mouth in 28 hours Tanret reactions still negative and patient still drowsy. T. 101° F. No vomiting or other gastro-intestinal symptoms. Quinine, gr. 10, intravenously. Tanret positive 5 hours later. T. 98° F. in 24 hours. Progress satisfactory. Tanret positive while dose of oral quinine remained at gr. 30 per day, but always negative during convalescence on any dose less than gr. 15 by mouth. Discharged on suppressive dose of gr. 15 of quinine daily in place of previous gr. 5.

TANRET REACTIONS IRREGULARLY POSITIVE

CASE 8.—Aged 27. In WA 8/12 year; 5th attack. On quinine, gr. 30, by mouth Tanret reaction positive in only one of every 3–4 specimens of urine. No vomiting. No intravenous quinine given. T. 100–101° F. until 6th day. Recovery slow. In convalescence gr. 15 quinine by mouth necessary for positive Tanret. All reactions negative after gr. 5 and gr. 10.

CASE 9.—Aged 24. In WA 8/12 year; 9th attack. MT rings +. Tanret irregularly positive on gr. 30 oral quinine daily. No vomiting. T. 99·6–101° F. for 5 days. No intravenous quinine given. Recovery slow. In convalescence Tanret reactions negative after quinine, gr. 5, but positive after gr. 10, by mouth.

CASE 10.—Aged 27. In WA 1 4/12 year; 8th attack. Blackwater fever 6 years before. No vomiting, but Tanret positive at very irregular intervals only. T. 101° F. Diagnosis clinical. No intravenous quinine given. Recovery slow. T. 99–100° F. until 5th day. In convalescence Tanret reactions all negative until dose of quinine raised to gr. 15 daily.

CASE 11.—Aged 27. In WA 7/12 year; 4th attack. MT rings ++. Tanret irregularly positive on gr. 30 of quinine by mouth. After gr. 40 in 28 hours MT rings still ++. No vomiting. T. 99–100° F. for 6 days. No intravenous quinine given. In convalescence Tanret tests all negative after gr. 5 or 10 of quinine by mouth, but positive after gr. 15.

CASE 12.—Though this is the most extreme "non-reactor" of the present series, 2 similar examples have since been found in a period of 7 months. The history is given in greater detail than the others because of its unusual and illustrative features. Aged 21. In WA 1 year. Has had 12 attacks, each coming on a month after the previous one. Admitted 7th day after last attack with "low fever" and persistent debility. Hb. 70% (Haldane). T. 100° F. MT rings +. Treatment: gr. 30 of quinine by mouth daily for 7 days, followed by gr. 10 daily. (We had not yet begun regular Tanret tests.) Three weeks after admission T. 99° F. Marked debility. Red cells 3,000,000 per c.mm. Treatment with gr. 30 of quinine daily resumed for 7 days. Tanret reactions positive at irregular intervals—less than one positive per day. No vomiting or other gastro-intestinal disturbance. At the end of course T. 99° F. Red cells 3,200,000 per c.mm. Quinine increased to gr. 45 daily (3 doses of gr. 15) for 5 days. Slight increase in number of positive Tanret reactions, but still irregular. Red cells 3,580,000. Quinine stopped for 24 hours. Tanret reactions all negative. *Quinine, gr. 10, given intravenously but Tanret reactions still negative throughout the subsequent 24 hours.* Quinine increased to gr. 60 daily by mouth (3 doses of gr. 20) for one day only. For the first time since admission signs of cinchonism appeared in the form of tinnitus, deafness and some giddiness. Tanret reactions were, for the first time, positive throughout 24 hours. Quinine reduced to gr. 45 daily by mouth for 4 days. Tanret remained positive over this period and the signs of cinchonism continued. Marked subjective improvement. T. 98·4° F. Red cells 4,800,000. Quinine reduced to gr. 30 daily by mouth (3 doses of gr. 10) for 5 days. Signs of cinchonism disappeared and Tanret again became irregularly positive. Quinine reduced to gr. 20 daily by mouth (2 doses of gr. 10) for 3 days. All Tanret reactions negative on this dose.

Various doses of quinine were tried before the suppressive dose was ultimately fixed at gr. 40 of quinine by mouth (2 doses of gr. 20). On this amount Hb rose to 88% and Tanret reactions were positive daily in about two-thirds of the specimens. Cinchonism was absent. The patient was sent out of the tropics, since this appeared too large a suppressive dose to be continued, in spite of the fact that he felt fit for the

first time since arrival in West Africa and wished to return to duty.

OBSERVATIONS DURING CONVALESCENCE

From the 12 histories quoted above it will be noted that 6 men (cases 7–12 inclusive) required, during convalescence, a dose of quinine by mouth greater than the prescribed daily suppressive dose of gr. 5 before even a single positive Tanret reaction could be demonstrated in their urines in the next 24 hours. Twelve others, with the same deficiency, were found among the 88 whose Tanret reactions during treatment of the acute attack with gr. 30 daily had been regularly positive. In all, therefore 18 soldiers out of 100 excreted no quinine in their urines for 24 hours after the suppressive dose they were ordered to take. The minimum doses required to produce even one positive Tanret reaction in these 18 men were: gr. 40 for 1 man; gr. 15 for 7 men; and gr. 10 for 10 men. Unfortunately, the number of attacks is not known for all these 18 men, but reference to the histories of cases 7–12 shows that these 6 soldiers had all suffered too numerous attacks for their safety—a total among them of 45 attacks in a period of 72 months—an average of over 7 attacks per man per year.

CONTROLS

As controls we studied 53 soldiers who were at the time of the test in good health, whose blood-films were free from malaria parasites and whose hæmoglobin readings were over 80% (Haldane scale). Of these men, 33 had suffered one attack (but not two) of malaria while the remaining 20 had had no malaria as far as could be discovered. No difference in the Tanret reactions was found between those who had and those who had not passed through an attack of malaria. None of the men had been less than 6 months in West Africa, and all had taken a suppressive dose of gr. 5 of quinine daily since arrival.

Procedure.—All urines were examined before the test and gave a negative Tanret reaction. The men then swallowed, under our personal observation, a dose of gr. 5 of quinine in solution. They reported at 15, 30 and 60 min. after the test-dose and then at hourly intervals in order to pass urine for examination. After a strong positive reaction appeared we stopped the hourly examinations, but did a final test in each man 24 hours after the dose of quinine.

All the 53 men showed strongly positive Tanret reactions within 5 hours of taking the quinine, but all the urines again became negative within 24 hours. There were great individual differences as regards the appearance and duration of positive reactions. None were positive at 15 min., 5 at 30 min., 15 at 60 min. and the remaining 33 between 2 and 5 hours. We did not follow the disappearance of the positives in all cases, but of 5 we did examine all were negative again within 10 hours.

DISCUSSION

Checking administration by Tanret tests.—One of the commonest misapprehensions regarding the Tanret test is that a positive reaction is obtained in the urine within 15 min. of taking a dose of quinine and that the reaction persists for the rest of the day. Thus Byam (1922) alleged that 70 out of 100 pensioners under treatment for malaria were not taking their quinine because he found a negative Tanret reaction in that number, which he says would have been impossible "had even a five-grain dose been taken and absorbed within the previous 24 hours." The French anti-malaria mission in Salonica (1918) acted upon a similar assumption. As Wenyon (1921) confirms, a French soldier could be asked to produce a specimen of urine *at any time* for a Tanret test. A single negative reaction was held to prove that the man had not taken his prophylactic tablet of quinine (gr. 6). Had we relied upon no more than a single examination at say 1 hour after the dose had been taken—a common procedure—we should have recorded only 37·7% (20 out of 53) as positive, whereas by continuing the examinations at hourly intervals up to 5 hours we found that all of 53 soldiers in normal health who had taken gr. 5 of quinine under supervision gave positive reactions.

Controlling therapy of acute attacks by Tanret tests.—In our 100 men, every patient who showed positive Tanret reactions in all urines during treatment rapidly recovered from his fever. On the other hand, when Tanret reactions were completely absent during the treatment by mouth (cases 1–7) the patients were all acutely, even dangerously, ill. Administration of intravenous quinine to such men was always followed by a rapid improvement in health, accompanied by positive Tanret reactions in the urine. Thereafter ordinary doses of oral quinine were enough to control the fever and maintain the positive Tanret reactions. We believe that the Tanret reaction, used in this way, is a simple and reliable guide to discover men who require parenteral quinine. It will be noted that vomiting and gastro-intestinal disturbances—usually given as important indications for parenteral quinine—occurred in only one (case 4) of the 7 patients with completely negative Tanret reactions. This raises a question, how far non-absorption is sufficient to explain the failures of oral quinine to bring the fever under control—a point we shall refer to later.

In 5 men (cases 8–12) the Tanret reactions, though not completely negative as in cases 1–7, were most irregular. Nevertheless, these soldiers were not given intravenous quinine to control their acute attacks, partly because they were not so dangerously ill and partly because we wished to compare their progress with cases whose Tanret reactions were positive in all urines. Recovery was distinctly slower both as regards duration of pyrexia and disappearance of symptoms, and in future we gave parenteral quinine to patients of this type.

It is of interest that in the acute illnesses where we gave a single dose of intravenous quinine, sufficient to control the infection, the subsequent Tanret reactions were positive on oral quinine in doses which had been previously insufficient to produce such a result. This finding fits observations and practice of earlier workers, which do not appear to have sufficiently influenced the courses of quinine generally advised today. Manson-Bahr (1931) recorded that "heroic" doses of quinine might be required to save life, but that when such doses had brought the disease under control smaller amounts sufficed to continue treatment. Stitt (1919) quotes Torti's experience in the Panama zone that large doses of gr. 45 of quinine daily should be given "at the commencement of treatment." Deeks (1925) advised up to gr. 60 of quinine a day for the first 2 or 3 days. It was only by this means that any progress was made in treating case 12.

These doses are not, of course, required everywhere. Nicol and Shute (1942) writing—as they emphasise—of people returning to England, have described the control of subtertian malaria with very small doses of quinine. Even in West Africa the disease appeared to differ in different localities in its severity and in the doses of quinine required for its treatment. In many parts of the world, however, patients are often found who are difficult to treat successfully, and in consequence speculation about "quinine resistant" strains has arisen. We have not met "quinine resistance" and believe that treatment controlled by the Tanret test, as we have described, would do much to cut out this bogy.

Tanret test in fixing daily suppressive doses of quinine.—Where, as in hyperendemic areas, daily suppressive treatment is a necessity, it is important to use the minimum effective dose. We believe that this may be influenced by factors of locality, climate, strain of malaria and duties. Individual differences of quinine absorption, metabolism and excretion would also appear to play a part, and it seems important that a high attack-rate was found in those of our convalescents (cases 7–12) whose daily dose (gr. 5) of quinine was insufficient to give positive Tanret reactions in their urines. Parsons (1922) thought that individual factors accounted for some of the alleged failures of prophylactic (now called "suppressive") quinine. He quotes a "Macedonain observer" as having stressed the need to determine the optimum dose of suppressive quinine for each locality and strain of parasite.

Quinine excretion and blackwater fever.—Of the 12 men described above, 3 have some association with blackwater fever. Cases 2 and 5 are known to have developed blackwater fever 6 and 7 months after our observations; case 10 had suffered from the disease 6 years before. Outside the 100 soldiers referred to, we have been able to examine 2 blackwater fever convalescents who both required gr. 15 daily to produce

positive Tanret reactions. By the time these facts had raised in our minds the question of a possible association between some abnormality of quinine metabolism and blackwater fever, the opportunity had passed to make further observations.

The number of attacks of malaria, which the Tanret negative cases have passed through, obviously brings them to the point of "continuous infection" which is commonly regarded as a "pre-blackwater" stage. Ramsden, Lipkin and Whitley (1918) studied the quinine content of blood and urine in a patient during two attacks of blackwater fever and found in both attacks values for urinary quinine much below those of normal patients, even after renal function tests were normal.

Cause of negative reactions.—Possible causes of the negative reactions are:—

Evasion: We were fully aware of the way in which soldiers evade doses of quinine and took precautions—described in the text—to ensure that this was not the explanation in our patients.

Non-absorption: This is the commonly accepted explanation but we feel that, whatever part it may play, it is not the complete answer. Vomiting or other gastro-intestinal disturbances occurred in only one of the 12 patients described and in none of the convalescents. Patients with acute and chronic amœbic and bacillary dysentery, achlorhydria and peptic ulcer gave positive Tanret reactions on normal doses of quinine. Finally, in case 12, the most difficult in which to produce positive reactions, a negative Tanret followed even an intravenous injection of quinine.

Errors of quinine metabolism: Previous workers have referred to this question. Ramsden and Lipkin (1918) state that concentrations of quinine in the blood of chronic malarial subjects are always much lower than in healthy men taking the same dose of the drug. Wenyon (1921) referred to the difficulty of treating chronic malarial subjects who had been treating the disease by continual dosing with quinine, and suggested that the body might have acquired some capacity to get rid of or store up quinine so that it failed to reach the parasites at all. Fletcher (1923), investigating alleged failures of quinine, mentioned the possibility of excessive destruction of the drug in the tissues, perhaps more marked during acute attacks or as a result of prolonged subclinical infection. Ramsden, Lipkin and Whitley (1918) showed that extracts of liver in vitro could destroy quinine.

If excessive destruction of quinine by the tissues be accepted as all or part of the explanation of the poor excretion it may be that "heroic" doses in the early stages of treatment and parenteral quinine act in the same way by forcing the level of the drug in the blood to a point at which enough free quinine escapes destruction to kill the parasites and be excreted in the urine as in the ordinary case. Where quinine is not pushed to these levels the excretion apparently remains impaired, even in convalescence, and the efficacy of the normal suppressive doses may be so lessened as to favour frequent recurrences (cases 7–12).

We regret that we had not the facilities to do quantitative estimations of quinine in blood, urine and other excretions, in an effort to take these views beyond the realm of speculation.

It is of interest to note that Bryant (1942) in treating subtertian malaria in the Sudan with atebrin found that to control severe malaria it was necessary to administer atebrin in much larger doses than are usually recommended and that he formed the opinion that the lethal action of atebrin on the parasites was not marked until the renal threshold of the drug had been reached; when the urine became bright yellow, the temperature fell and the patient immediately improved.

SUMMARY

Tanret tests for quinine were done on all urines of 100 British soldiers admitted to hospital suffering from subtertian malaria in Southern Nigeria and on 53 men in normal health.

Reactions were examined during acute attacks treated by gr. 30 of quinine by mouth daily for 7 days, and during convalescence after the daily suppressive dose of gr. 5. Precautions were taken to ensure that the drug was swallowed.

Of the 100 patients, 88 who showed positive reactions in every urine during treatment of the acute attack made rapid recoveries.

After gr. 5, all the 53 normal men showed positive reactions, but these did not appear within 15 minutes and persist for 24 hours as they are commonly supposed to do. Only 20 men showed positive reactions within an hour, the others became positive between 1 and 5 hours.

By comparison with these standards some deficiency of quinine excretion was shown by 24 of the 100 men; 6 were deficient only in the acute attack, 12 only in convalescence and 6 in both acute attack and during convalescence.

In 7 men quinine was absent from all urines during the acute attack. They remained seriously ill until given intravenous quinine; then they showed positive Tanret reactions in all urines and recovered rapidly. Only one had negative reactions in convalescence.

A group of 5 men who showed positive reactions at irregular intervals during the acute attack recovered slowly and showed negative reactions during convalescence.

The 6 men whose excretion was deficient both in the acute attack and during convalescence had all suffered repeated attacks at short intervals.

The findings are discussed and their relation is considered to the condition of "continuous infection," which commonly precedes blackwater fever. The need for adjusting quinine courses in individual cases in relation to quinine metabolism is emphasised.

CONCLUSIONS

Despite precautions to ensure that quinine was being regularly taken, 24 out of 100 malaria patients showed negative Tanret reactions in all or many of their urines during treatment and convalescence.

Their responses to quinine treatment compared unfavourably with those whose Tanret reactions were regularly positive.

It is suggested that quinine administration and dosage in treatment and daily suppression (prophylaxis) should be controlled and adjusted for each individual by using the simple Tanret test in the way described.

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PLASTER TECHNIQUE IN FRACTURES OF THE TIBIA AND FIBULA

THE SWALLOW-TAILED ANTERIOR SLAB METHOD

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FRACTURES of both bones of the leg constitute one of the commonest injuries at the present time, both in civilian and service casualties. The object of this paper is to describe a method of applying plaster which has been found extremely useful in such cases. Its advantages are that it gives the surgeon complete control over the fracture at all stages without the use of special apparatus and with the minimum of skilled assistance. At the same time, it gives such freedom of access and manœuvre for the application of the plaster that the most accurate moulding can be obtained. These advantages have an added value at the present time, when surgeons may have to work single-handed under conditions which preclude the use of complicated apparatus. The method was originally devised for use in the operating theatre but it is now used in my clinic as the standard method for all "long leg" plasters.

Most fractures of the tibia and fibula with displacement can be so accurately reduced by manipulation that they remain stable to gentle impaction—that is, they do not become redisplaced when the fragments are gently pressed together. This applies even to many so-called "unstable" oblique varieties, for there are often ledges or notches on the fragments which can be engaged to produce a reasonably stable reduction. Manipulation must be done early, however, before swelling makes palpation difficult, and it must be done under the full relaxation of anæsthesia. Those oblique fractures which are genuinely unstable will require either traction or internal fixation (my own preference is for the latter) but in either case the subsequent application of a plaster cast will be rendered much easier by the method to be described. A recently reduced fracture may easily be redisplaced during the application of plaster if there is any movement of the limb. It is for such cases that the present method is most useful, for not only does the limb "stay put" from the moment of reduction to the completion of the plaster, but the fracture can be controlled with ease and absolute certainty throughout the whole procedure. Finally, it is ideally suited to a patient on traction on a Thomas splint.

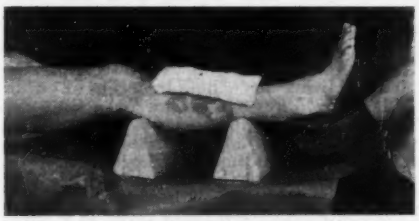

Fig. 1—Leg supported on wedges, with ankle held at a right angle.

The essential feature of this method is the use of an anterior slab, fashioned in such a way that once it sets it effectively fixes the whole leg. 'Cellona' is suitable for the purpose, because of its quick setting properties and the ease with which a dry "tailored" slab can be prepared. The exact technique is as follows:—

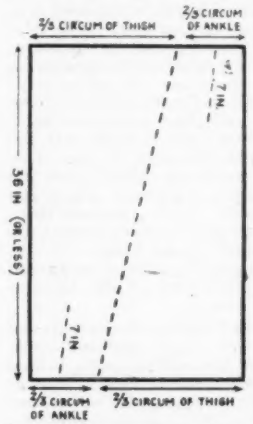

Fig. 2—Pattern for swallow-tailed slab.

Anæsthesia is induced either by low unilateral spinal or by continuous intravenous 'Pentothal.' The fracture is then accurately reduced, the test of this being its stability to gentle impaction. The leg is then placed on two wooden wedges 5 in. high as shown in the illustration (fig. 1.) The upper one is placed just distal to the knee-joint and the lower one at the level of the fracture. A block or sandbag can then be placed under the heel, arranged at such a height that the alignment of the fracture is correct when viewed from the side. These wedges can be made easily by the hospital carpenter or handyman but if they are not available, a Thomas wedge or a hernia rest make convenient substitutes. It will be found that with the leg supported in this position the knee-joint assumes the optimum position for immobilisation—i.e., 10°–15° of flexion. The surgeon, standing at the foot of the table, can then correct any valgus or varus angulation by simply shifting the heel either medially or laterally. Rotation at the fracture can be easily controlled by holding the foot as shown in fig. 2, with the ankle-joint supported at a right angle. If an assistant or nurse experienced in the use of plaster is available the surgeon may prefer to hold the foot himself, but it is so easy to maintain reduction once the limb has been properly positioned that it may safely be handed over to the assistant if the surgeon prefers to apply the plaster himself.

The basis of the plaster is an anterior "swallow tailed" slab prepared as follows (fig. 2). In length it reaches from the upper third of the thigh to the sole of the foot. Its width at the upper end is equal to two-thirds of the circumference of the thigh at that level, and it tapers to a width at the lower end equal to two-thirds of the circumference of the ankle just above the malleoli. The narrow end of this slab is slit up the middle for a distance of 7 in. in order to form two "tails." If cellona material is used, 6 layers thickness will give adequate strength, but will be thin enough to allow accurate moulding round bony prominences. Material 36 in. wide will usually be found to afford the right length of slab, and is economical if cut in the following manner:

The width of the material is used to form the length of the slab. The measurements at the thigh and ankle are taken and added together. This measurement is then marked off and the material folded on itself to make a rectangular slab three layers thick. The measurement at the thigh is marked off at one end of this slab, and the measurement at the ankle at the other end. An oblique cut is then made from one to the other, thus providing two tapering slabs each of the correct dimensions. These are then superimposed to give a slab six layers thick without any waste of material. Should 36 in. be too long, the "off cut" can be rolled into a circular bandage.

Fig. 3—Slab applied.

After soaking in tepid water and smoothing out all air bubbles, the slab is applied to the front of the thigh and leg, the two tails being moulded accurately over the malleoli and brought round the sole to overlap in the form of a letter U (fig. 3). Wet muslin bandages are then applied from the malleoli to the top of the slab in order to fix it, leaving only two small gaps where the wedges support the limb. In a few minutes the slab will have set and will be found to grip the whole limb so securely that the lower wedge and the support under the heel may be safely removed, the assistant holding the foot up by the toes while a posterior slab and foot platform are applied in the usual way and fixed by a spiral bandage. Finally, the wedge under the knee is removed and the leg held up while a posterior slab is applied from the calf to the upper end of the plaster and fixed by a couple of spiral bandages, thus completing the cast.

BLOOD-PICTURE AFTER MASSIVE TRANSFUSION

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THE following case throws doubt on two current theories—the first that large transfusions of group O blood into patients of other groups can reverse the blood-group; the second, that transfused serum agglutinins are neutralised by agglutinogens either in the blood cells, the serum or the fixed tissue cells of the recipient and that nothing more is needed to explain the absence of ill effects following transfusions with high-titre serum.

CASE-HISTORY

A woman of 50, actively engaged as an industrial welfare worker, felt faint after a light meal and immediately vomited a large amount of blood. During the night she had two further severe hæmatemeses and fainted. She was admitted to King Edward Memorial Hospital, and was immediately grouped, found to be group B (3) and transfused with four pints of group O blood after cross-matching of each bottle against her serum. The following morning her hæmoglobin was found to be still only 65% (Haldane). During the next six days she had six further attacks of hæmatemesis

and continuous melæna, and during this time, by continuous drip, she received 14½ pints of blood as well as considerable amounts of saline, given to keep the needles open between bottles of blood. In spite of this, on the seventh day of her illness, her hæmoglobin had fallen to 30%. During the next four days she received a further 8½ pints which brought her hæmoglobin up to 60%, when transfusion was stopped. She had received 23 pints in all, 22 of group O, and one—the ninth—of her own group B.

Since there were five other cases with severe hæmorrhages in the wards at the time, the house officers were so overworked that they had no option but to continue to transfuse with stored group O blood, believing that they ran the risk of killing the patient if they continued, but certain that she would die if they stopped.

There were two reactions: the first, a typical rigor, with the 8th pint; and a mild reaction with a sense of fullness in the chest and buzzing in the ears with the 23rd. There was never any jaundice, nor any urinary changes.

I was able to examine her blood a week after her last transfusion. Some of her corpuscles still reacted as group B. The serum in her contained no trace of agglutinins against known corpuscles of all four groups—that is to say, that one part serum to one part of a 2% saline suspension of corpuscles showed no agglutination microscopically after standing at 37° C., at room temperature or at 4° C. for 18 hours; for practical purposes she had become a universal recipient.

Clearly, had the agglutinins been merely neutralised by her serum or cells, the alpha agglutinins in the transfused blood and her own alpha agglutinins would still have been present. I anticipated that they would return gradually to whatever her normal would have been, and examined her blood again a week later and found that alpha agglutinins were present to a titre of over 1:1600. It was not possible to examine her blood again until her return from convalescence, six weeks later, when she had a normal blood-picture and her agglutinins had fallen to 1:64, which is probably her normal.

DISCUSSION

This case appears to dispose of the idea that it is possible to reverse the blood-group by using group O blood, and I find I am not alone in doubting this; Aubert and his colleagues (1942) expressed their scepticism and they receive support from Shamov (1940). A second point is that the disposal of the foreign agglutinins and the total suppression of her own was too efficient to be merely accidental. We must look at the only natural condition in which transfusion of agglutinins probably occurs—that is, between mother and child. I suggest that we have, in this case, a reversion to the intra-uterine conditions.

Evidence in support of this view can be deduced from a table in the paper of Lederer and his colleagues (1929) who analysed 500 pairs of mothers and children. Of the 126 children whose agglutinins would have been active against the mother's cells, all showed suppression of agglutinins, whereas 54% of those whose bloods were compatible with their mothers' developed agglutinins before birth; further, if agglutinins pass the placental barrier at all in man, and there is good evidence for this (Bourquin, 1921), then both incompatible and compatible agglutinins would pass to the child from the mother; and though it might be possible to explain the absence of the incompatible ones by a process of simple neutralisation by the appropriate agglutinins in fixed tissue cells or serum, yet a proportion of the children appear to dispose of all agglutinins irrespective of whether incompatible or compatible, and whether derived from their mothers or produced in their own bodies—a condition analogous to that seen in this case. Hirszfeld and Zhorowski (1925) suggest that this adjustment between mother and child is reciprocal, there being a tendency for the mothers producing agglutinins against their own infants to suppress them.

A less fantastic theory has been suggested to explain the present result; it is that among the donors used was a weak group A, misgrouped as an O, and that the changes seen were due to the immunity reaction following this. To meet this suggestion the history of the local donors was investigated. All but 2 had been used three or more times before and had been tested on at least four occasions. The remaining 2 were retested both as to agglutinins and agglutinogens. All have been retested since and their bloods used for other transfusions without a weak group A being detected. The donors not known directly to us were tested and bled by the Slough Depot and the blood retested by us. Apart from this, the change seen in this case is greatly in excess of that following any single injection of either incompatible blood or high-titre serum of a different group, since here the fall in agglutinins is to zero, whereas in the comparable cases of incompatible transfusion the whole cycle of reaction occupies a shorter time and the base line is not, apparently, reached.

This type of reaction had not yet been obtained with ordinary large transfusion of 4–6 pints given in a short time.

SUMMARY

A case is reported in which transfusions of 22 pints of group O blood and one pint of group B into a patient of group B, not only failed to reverse the blood-group but entirely suppressed all agglutinins in the recipient's blood for at least a week. This may be comparable with the suppression of agglutinins in the fœtus.

I wish to thank Dr. J. B. Harman for the clinical notes.

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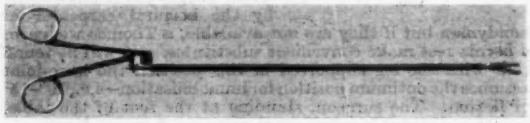
New Inventions

MALLEABLE FOREIGN BODY FORCEPS

THE advantages which might be expected from putting forceps jaws at the end of a malleable pewter probe led to the production of the following instrument. The first model was made in the field by putting a screw thread on one blade of an old pair of Spencer-Wells and screwing on a pewter anæsthetic tube. To the other end of this tube was attached jaws of a small pair of forceps, cut out from one prong of an electric-light plug, and activated by a wire passing down the lumen of the tube to a notch in the unattached shortened blade of the Spencer-Wells. This instrument has been useful in removing calculi from the calyces of kidneys or the ureter, especially when the organ cannot easily be delivered. It also proved valuable in palpating and removing metal or bony fragments from narrow and tortuous wounds along which straight forceps will not pass. This model has been improved and made presentable by Mr. Schranz of the Genito-Urinary Manufacturing Co.

The jaws consist of one fixed blade attached to the shaft and one movable blade. The blades are ¼ in. long and $\frac{3}{16}$ in. broad, rounded at the end, with fine smooth teeth, behind which the surface is recessed. The movable blade overhangs the fixed, thus producing the maximum gripping power, but with the minimum likelihood of damaging mucous membrane.



The movable blade can be made to swing through 60° or more (¼ in. gape), the range being adjustable. The shaft is a copper tube 10 in. long and $\frac{5}{32}$ in. in diameter (equivalent to a 14 French catheter). It bends readily, but when bent is more rigid than a pewter probe. The handles lie in the same axis as the shaft, in order to simulate closely the ordinary type of forceps, so that their manipulation and feel is as natural as possible.

The advantages of the forceps are these. The shaft can be bent into almost any shape that a pewter probe can be and the terminal forceps can still move through

their range of movement and give a firm grip. Each calyx of a short pedicled kidney can be fully explored with the same instrument, with the least chance of damaging the mucosa. The jaws of the forceps work with precision and delicacy and yet give a firm retentive grip. Its blunt end and small diameter makes it a useful probe, and gives an excellent metallic or bony "feel" which makes it particularly valuable in exploring deep wounds. It can be readily passed along an examining finger and can often be employed to grip a foreign body at the bottom of a tortuous sinus when the ordinary forceps cannot be made to open sufficiently.

St. Paul's Hospital, Endell Street. J. E. SEMPLE, MD CAMB, FRCS Major RAMC.

Medical Societies

SOCIETY OF MEDICAL OFFICERS OF HEALTH

AT a meeting of the Fever Hospital Medical Service Group on July 16, with Dr. ANDREW TOPPING in the chair, a discussion on recent advances in the

Laboratory Control of Typhoid and Paratyphoid

was opened by Mr. A. FELIX, D SC, FRS, who outlined the theory and practice of the two recently introduced laboratory methods—typing of typhoid and paratyphoid B bacilli by means of Vi-bacteriophage, and Vi-agglutination tests as an aid to the detection of chronic typhoid and paratyphoid B carriers. Craigie and Yen (1938) found that strains of the typhoid bacillus can be divided into a number of types on the basis of their sensitiveness to specifically adapted anti-Vi bacteriophages. Typing by this method is as reliable as that obtained in streptococcal or pneumococcal infections by the old-established serological tests. This year, Felix and Callow have found that the bacteriophage technique can be applied also to strains of the paratyphoid B bacillus. Anti-Vi phages of *Bact. paratyphosum B* can be adapted to develop a high degree of specificity for particular strains, whereas anti-O phages are incapable of such adaptation. So far four different Vi-phage types of *Bact. paratyphosum B* have been identified, and more than 90% of the strains isolated from patients and carriers in Great Britain during the past three years were found to belong to those four Vi-phage types. The new typing method is an indispensable laboratory aid to the investigation of sporadic cases or outbreaks of typhoid and paratyphoid B fever. The detection of a chronic carrier is usually difficult, though the methods of isolating typhoid and paratyphoid bacilli have been greatly improved through the introduction of refined culture media. In all the recent outbreaks of paratyphoid B fever in this country the persons responsible for the spread of the infection were found to be temporary excretors. The true culprits—the chronic carriers—escaped detection. The Vi-agglutination test, which originally applied to typhoid alone, has now been extended to paratyphoid B fever. Dr. Felix demonstrated that this test can be used as an aid to the detection of chronic carriers among recovered patients, who otherwise might be discharged from hospital because of the intermittency in the excretion of bacilli. A decreasing Vi-titre will indicate temporary excretion, whereas a steady or rising Vi-titre will arouse suspicion as to a possible chronic carrier state. Dr. Felix expressed his belief that the laboratory methods now available enable the public-health authorities to reorganise and intensify the fight against the chronic typhoid and paratyphoid carrier. Close coöperation between clinician, epidemiologist and laboratory worker now seems to promise to lead far towards the ultimate eradication of the enteric fevers.

Dr. W. H. BRADLEY (Ministry of Health) remarked that analysis is a major strategy of science and recalled that it is little more than a hundred years since Louis and Gerhard differentiated typhoid from typhus. William Budd of Bristol recognised typhoid as an alimentary infection in the middle of the nineteenth century, and since then enteric fever has been split up into a number of groups—first by the identification of the typhoid bacillus by Eberth in 1880, and then by the recognition of the para-organisms and the other salmonellas at the turn of the century. Now by the application of the power of certain bacteriophages to lyse the organisms of typhoid and paratyphoid it is possible to make a further analysis into a considerable number of "phage types" and a new era in the epidemiology of the enteric infections is opening. Dr. Bradley illustrated the application of this new method to epidemiological field studies. He showed how at one time a number of cases of typhoid appeared in a cathedral town in the south-west. This group would have defied investigation had it not been found that they belonged to three different phage types; when studied on this basis they proved to originate in three separate sources of infection operating simultaneously. It was possible to trace these sources to separate foci outside the city. More recently, 14 cases of typhoid occurred in an extra-metropolitan borough using its own water-supply, which naturally came under suspicion because an alternative common aliment could not be identified. The appearance in a neighbouring borough of 2 more cases of typhoid of the same type in persons who had not consumed the suspected water helped to remove suspicion from the water-supply. It is usual for single cases, apparently sporadic, to occur in a borough from time to time. For example, although only about 50 cases of typhoid were notified in London in 1942 they occurred in 22 of the 28 boroughs. It is rarely possible to trace the source of infection or to relate cases arising in different boroughs. Since the beginning of 1943 an attempt has been made to apply phage typing to this problem. Up to June cases of typhoid have appeared in 10 boroughs. The great majority of these have been related to three foci of infection. Of the remainder, 2 cases were imported, another arose in a mental hospital and one only proved resistant to investigation. Dr. Bradley supported Dr. Felix's opinion that with careful and persistent epidemiological inquiry and specialised bacteriology it should now be possible to account for almost every case and in time to eradicate completely the enteric fevers, but certain changes in current practice are necessary. Hitherto the bacteriological objective of clinicians was to obtain sufficient negative cultures to clear the patient; now the indication is to perform immediate and repeated blood, stool and urine cultures until the organism is recovered and typed. The organism from every sporadic case and from a sample of the cases in any outbreak should be typed. It is also desirable that clinicians, taking into account the clinical development of the disease, should determine the date of onset as accurately as possible and should communicate this date and also the type of organism infecting the patient to the medical officer of health investigating the source of the disease. Dr. Bradley thought there is some clinical evidence that organisms of different types differ also in virulence, and to some extent typing may be of prognostic value. He also recommended the use of Vi determinations in the detection of carriers. As a preliminary screen for a carrier, in a food-handling establishment for instance, the Felix Vi-test simplifies investigation enormously. Taken in conjunction with the evidence obtained from circumstantial inquiry, this screen eliminates a large part of the need for wholesale stool and urine culture, and gives a prompt and more dependable answer.

Dr. ROBERT CRUICKSHANK (LCC) thought that the crux of the situation is the chronic typhoid carrier. Recovery of typhoid and paratyphoid organisms either in the acute stage of the disease or in convalescence demands the use of selective media. This is true over the whole range of bowel infections. Their use, for example, has demonstrated that convalescent carriers occur after salmonella infections, a thing never suspected in the past when MacConkey's medium was employed.

Dr. A. L. K. RANKIN (Twickenham) described the clinical features in the small extra-metropolitan borough outbreak mentioned by Dr. Bradley. In the adult cases the onset was gradual but 2 children had a gastro-intestinal onset. A characteristic of all cases was their mildness. During the stage of advance the temperature showed marked morning remissions, which Dr. Rankin regards as a good prognostic sign. Leucopenia was present in all cases. The diazo test was consistently negative but no case was admitted before the 14th day

of disease. One woman developed the uncommon complication of mastitis.

Colonel G. W. M. FINDLAY wondered if it would be possible to treat typhoid by phage given intravenously. In India dramatic results were claimed by the combined use of phage and typhoid antitoxin to deal with lysed products. In mouse experiments he has found it necessary to give phage very early to obtain a therapeutic effect.

Dr. BRADLEY, in reply to a question, said that gastro-intestinal symptoms at the time of ingestion of typhoid bacilli are common—they were encountered both in the Croydon water-borne and the Bournemouth milk-borne outbreaks. Intestinal symptoms, consisting of the passage of blood and mucus, are usual to begin with—vomiting comes later. The whole upset is usually over in 48 hours. He described an hotel outbreak where 36 guests had gastro-intestinal symptoms within 48 hours of arrival and 17 subsequently developed typhoid.

Dr. FELIX suggested that the gastro-intestinal symptoms are not necessarily due to typhoid or paratyphoid organisms. They may indicate only that the vehicle is heavily contaminated with other organisms, including preformed toxins. He agreed with Colonel Findlay that in the phage treatment of experimentally infected mice the results are good in typhoid whereas no effect can be seen in aertrycke infections. This is probably because typhoid is not a usual infecting organism in mice whereas aertrycke is. He has used phage in large intravenous doses in the treatment of chronic typhoid carriers but the experiment was a complete failure. Yet the same phages had been tested in broth and up to 50% ox bile where they produced complete sterilisation. He thought that phage treatment might be tried on carriers of shorter duration where there is less heavy damage at the local focus of infection.

Reviews of Books

Pulmonary Tuberculosis

HANS JACOB USTVEDT, MD Oslo, first assistant physician to the State Hospital, Oslo. (Bale. Pp. 252. 25*s*.)

THIS book is based on a series of lectures delivered by Dr. Ustvedt to medical students at the University of Oslo, and though it is primarily intended for the undergraduate reader it should inform a much wider circle, for it contains an account of the Norwegian, or more strictly the Scandinavian, view of the natural history of tuberculosis. It has been divided roughly into three parts: tuberculous infection; progressive pulmonary tuberculosis (phthisis), and treatment, with an additional chapter on miliary tuberculosis and prophylaxis. The section on infection (of which the Norwegian school of phthisiology has made a particular study) is as lucid an exposition as can be found anywhere. The original work of Heimbeck, Scheel, and Ustvedt himself is freely quoted in accounts of the clinical manifestations of the primary complex, the significance of tuberculin testing and of erythema nodosum, and the time-relation between infection and disease. The steps leading to the early recognition of established disease are well set out, but the demonstration of tubercle bacilli in the fæces is not given its fair share in the diagnosis. The many pitfalls in the diagnosis of tuberculous cavities and of radiological opacities in the region of the lung root are well discussed.

The author's bias in treatment is towards methods of collapse, which are placed before general or constitutional measures. In so far as this emphasises the need for early diagnosis there is something to be said for it, provided the impression is not created that the sanatorium routine is of secondary importance. No praise of this good book would be complete which did not include the fine translation by Dr. A. L. Jacobs.

Physiological Principles in Treatment

(8th ed.) Sir WALTER LANGDON-BROWN, MD CAMB., FRCP; REGINALD HILTON, MD CAMB., FRCP. (Baillière. Pp. 323. 12*s*. 6*d*.)

THIS book is pleasantly written, with sufficient personal and historical allusions to merge it into the general development of British medicine. The emphasis is on treatment, and though the physiologist might complain that scientifically it is not analytical enough, and is too freely interpretive, the practitioner is safeguarded from undertaking any treatment based on theoretical considerations alone: as the authors point out, principles and not details of physiology are the foundation for their work and they give these clearly. Sometimes they seem to be unaware of a recent development, sometimes they are able (as in the case of renin) to show it is not really new; but they always preserve a sense of proportion, and—as its 34 years' record suggests—the book probably achieves its progressive object better by being brief, direct, and in the best sense conservative, than by a wordy advocacy of passing scientific applications.

Out of Working Hours

HENRY YELLOWLEES, DM, FRCP, DPM. (Churchill. Pp. 152. 8*s*. 6*d*.)

Dr. Yellowlees is a gifted occasional lecturer who succeeds in his aim "to say something practical, helpful and perhaps thought provoking about some branch or application of medicine, and to say it interestingly," in this collection of lectures. It would, however, have been more satisfying to the reader—as apart from the listener to whom they were first addressed—if some passages had been made more temperate. He calls psychological medicine, for instance, "the greatest and the most important and the most difficult and the most personal branch of medicine": perhaps it is, but surely this belongs to the "provocative generalities" which in the previous sentence he had deprecated. The medical and still more the general public can, however, learn from these vigorous addresses much about the broad aspects of mental hygiene, as well as something about the temperament and outlook on life of the distinguished psychiatrist who delivered them.

Institutional Care of Dependant Children in New Zealand

H. C. MATTHEW. (Oxford University Press. Pp. 141. 6*s*.)

THIS book, no. 18 of the publications of the New Zealand Council for Educational Research, describes a survey carried out since the war in institutions run by some of the religious bodies in that country. Mr. Matthew reviews the methods of other countries, lays down standards for institutions, and then describes what he found in those he visited, dealing with their buildings and administration, and the physical care and social life experienced by the children. The survey shows how far the problem of the dependent child is from being solved even in material things. We read of barrack-like conditions, of an interminable inheritance of second-hand clothes, of lack of contact with ordinary children and ordinary homes, and of the opportunity for handling money. The survey strengthened his conviction that institutional care should be avoided wherever possible. Like mental defect, dependency is a vast and persistent problem and we are only too willing to put it behind institution doors, comfortably out of sight, and forget about it, salving our consciences by buying a flag now and then. Mr. Matthew should go further and carry out a comparable study of foster homes, but the method should not be too objective. A woman brought up in a public assistance home who refused to let her own child go to a similar institution said the two chief disadvantages were the favouritism and the constant changes in staff and inmates which left the girl with a feeling that she had no fixed place in the world. These defects are not mentioned.

Messrs. Heinemann are in the process of publishing a series of collected researches from the inoculation department of St. Mary's Hospital. The first two volumes, being papers by Sir ALMROTH WRIGHT on war wounds and clinical pathology, have already appeared; the third is the first series of his "Studies on Immunisation" (25*s*.) which appeared first in 1909 and is now reprinted handsomely, with every advantage of type and paper. The second series of these classic studies is now in the press.

VITAMIN THERAPY

IN CARDIOVASCULAR DISORDERS

The fact that cardiac disorder is one of the most serious features of beri-beri early suggested that hypovitaminosis B_1 might be concerned in cases of heart disease not so obviously related to nutritional deficiency. Since the cardiac picture in beri-beri consists of dilatation and hypertrophy, chiefly right-sided, with venous congestion, failure, and œdema, vitamin B therapy has been employed particularly for these manifestations. Illustrative of work reported may be mentioned the following:—

CLINICAL REPORTS

Among a group of 120 patients showing signs of cardiovascular dysfunction, particularly increased heart rate and congestive failure, a significant proportion had symptoms of hypovitaminosis B_1 and showed a good response to vitamin B_1 therapy.[1]

In 30 patients, with signs of myocardial damage, who received a diet rich in vitamin B_1, a degree of symptomatic improvement occurred considerably greater than was to be expected from previous experience with similar patients.[2]

Of 13 children—aged from 18 months to 4 years—with cardiac disorders associated with nutritional deficiency of a general nature, of vitamin B_1, or of protein, a considerable proportion improved under treatment with a good dietary, supplemented by a rich source of vitamin B_1, such as wheat-germ or rice polishings.[3]

In a study of cardiac dysfunction resulting from hypovitaminosis B_1, it was stated that early cardiovascular manifestations included palpitation, a sensation of oppression in the chest and precordial distress, dyspnœa on exertion, and arrhythmia. As a rule these symptoms were benign and regressed on the administration of vitamin B_1. Later changes were enlargement of the heart and cardiac insufficiency. To clarify the diagnosis in cases of heart disease in which hypovitaminosis B_1 is suspected, the authors recommend the administration of vitamin B_1.[4]

SUPPLEMENTARY VITAMIN B

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These facts explain its widespread recommendation by physicians in all conditions in which hypovitaminosis B is present, for example, neuritis of dietary origin, anorexia, constipation and gastro-intestinal atony.

1 *Trans. Assoc. Amer. Phys.*, 1936, 51, 341; Ann. int. med. 1937, 11, 104.
2 *J. Lab. Clin. Med.*, 1937, 22, 991.
3 *Amer. J. dis. Child.*, 1938, 55, 750.
4 *Hospital, Rio. de Jan.* 1940, 2, 231.

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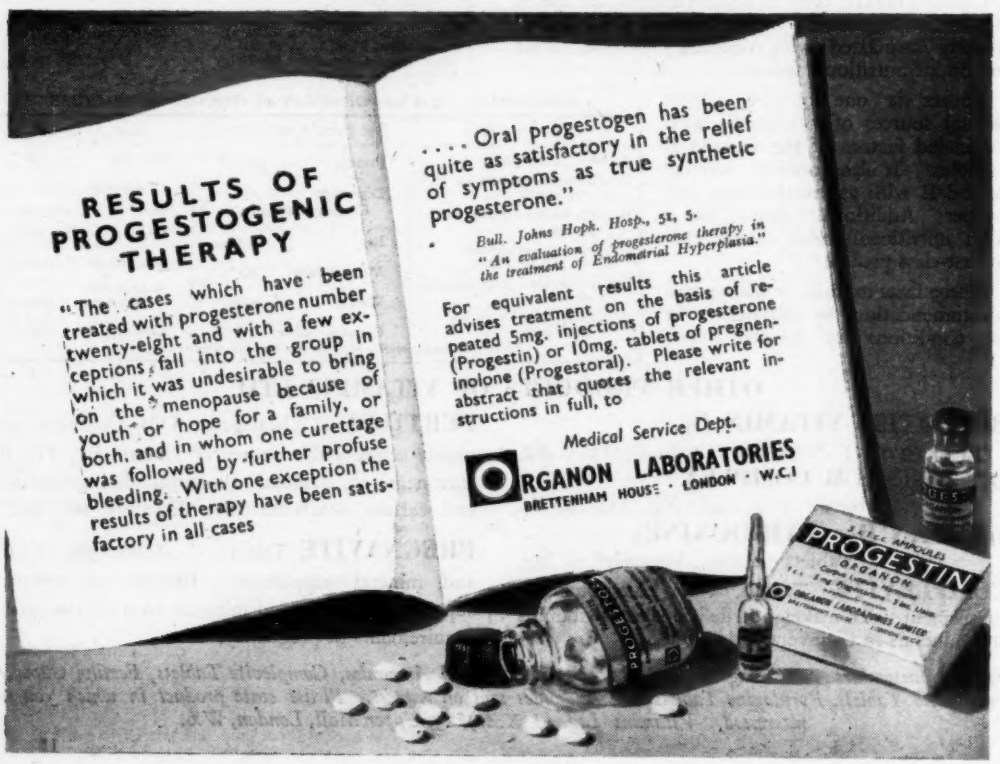
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Bull. Johns Hopk. Hosp., 52, 5.
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THE LANCET

LONDON: SATURDAY, SEPTEMBER 11, 1943

ANTITOXIC IMMUNITY

THIS war has seen the launching of large-scale campaigns for the defence of particular sections of our population against two enemies—diphtheria and tetanus—which are essentially toxin infections. In such infections control must be principally by prophylaxis, since toxin, once formed, quickly enters and destroys the cells in vital tissues; the clinical onset of infection is often insidious, so that therapeutic antitoxin may be given too late; and powerful antigens (toxoids) can be prepared from the toxins by the addition of formalin, which renders the toxin non-poisonous without affecting its antigenicity. It is obviously wiser therefore to protect the population at risk by active immunisation before they are intimately exposed, rather than give them a passive and temporary immunity by antitoxin after exposure or attempt cure after onset of the clinical infection. It may sometimes be desirable to combine both passive and active immunisation—for example, among the susceptible contacts of a family where diphtheria has broken out, or on the battlefield to ensure an immediate and high degree of resistance to tetanus. From the recent work of COOKE and JONES[1] it seems that, if this is done, the first injection of toxoid may with advantage be delayed for several weeks after the injection of antitoxin. Inevitably the adoption of large-scale active immunisation against diphtheria and tetanus has raised fresh problems, some of which can be solved only by practical experience. Nevertheless, the experimentalist in the laboratory can give useful pointers.

On another page HARTLEY and his colleagues at the National Institute for Medical Research provide some answer to two questions: Do adverse conditions, like shock, acute infection, exposure to cold and restricted diet, interfere with the body's capacity to produce antibody in response to an antigenic stimulus; and Does the boosting dose given some time after the primary inoculations provide the individual with a better residual immunity than he would otherwise have? The first question was prompted by the theoretical consideration that a shocked and wounded soldier, although actively immunised against tetanus, might fail to produce sufficient antibody to counteract any incipient infection with the tetanus bacillus. The results suggest that under a potent antigenic stimulus there is a good prospect of adequate antibody production even in the rigorous conditions of the battlefield, though a "shock" infection like gas gangrene may interfere to some extent with the response. What is still in doubt is whether the stimulus of natural toxin in a wound will provoke a sufficiently early and adequate antibody-response to protect susceptible nervous tissue against infection. HARTLEY's findings indicate that after an injection of toxoid a rise in the antitoxin level may be demonstrable as early as the 5th day, but ZUGER and his co-workers[2] demonstrated that immunised guineapigs infected with tetanus spores fail to show any increase in antitoxin until the 8th to 10th day. Indeed the response was often too late to prevent the onset of local or generalised tetanus. A smaller proportion of animals given an injection of toxoid at the time of infection developed local tetanus. It seems from these experiments that an actively immunised person with a low basal immunity may not escape clinical tetanus unless he is also given a protecting dose of antitoxin at the time of wounding, and this has in fact been an experience in the British Army.[3] If, however, this basal immunity can be kept at a higher level the risk of clinical infection will be greatly reduced. In a strictly controlled field test EVANS has established the investment value of a third dose of antigen to immunised persons. The graph which he has prepared from the antitoxic titres of persons given a boosting dose of tetanus toxoid 10 months after completion of the primary immunisation shows that 1½ years later the antibody content of their blood is at an appreciably higher level than that of those not given the *injection de rappel*. Since the boosting dose is now used in both the British and American Armies the chances of the wounded man contracting tetanus must be minimal. Here are lessons to be learned and applied in the immunisation of children against diphtheria.

Gas gangrene, another of the toxin infections, has not yet been brought to heel, and an incidence of 0·3% with a fatality of 50% among the wounded in the Middle East campaigns[4] suggests that active immunisation, if practicable, would be worth while among the armed forces. W. J. PENFOLD was an ardent believer in its practicability, and it is fitting that his pioneer work should be carried on by the Lister Institute. ROBERTSON and KEPPIE report in this issue that using as antigens concentrated and partly purified toxoids prepared by the bacterial chemists, they have been able to protect guineapigs against many lethal doses of the three common gas-gangrene anaerobes. As might be expected, best results were obtained against *Cl. œdematiens*, the most purely toxic in its action. Animals given a primary immunity by two injections at 3-weeks interval were as resistant to infection with this organism as others given an additional boosting dose, and this immunity was maintained for some months. Toxoid to *Cl. welchii* also produced a good primary immunity which could be reinforced by secondary immunisation; but as in tetanus the secondary response occurred more quickly after an injection of toxoid (3rd to 5th day) than it did with a natural infection (more than 5 days). Resistance to infection with *Cl. septicum* could not be easily induced by primary immunisation but the boosting dose gave a solid immunity. This protection afforded by an antitoxic immunity against an organism of considerable invasive activity corroborates the experimental results in the prophylaxis of gas gangrene with septicum antitoxin.[5] The Lister workers point out that for protection of animals against these gas-gangrene anaerobes a reasonable antibody-content is necessary, and no doubt, if active immunisation against gas gangrene becomes a reality, the boosting dose will be found as essential as it appears to be in the other toxin infections.

1. Cooke, J. V. and Jones, F. G. *J. Amer. med. Ass.* 1943, **121**, 1201.
2. Zuger, B., Greenwald, C. K. and Gerber, H. *J. Immunol.* 1942, **44**, 309.
3. Boyd, J. S. K. and MacLennan, J. D. *Lancet*, 1942, ii, 745.
4. MacLennan, J. D. *Ibid*, 1943, ii, 63, 94, 123.
5. Craddock, S. and Parish, H. J. *Brit. J. exp. Path.* 1931, **12**, 389.

DOCTORS AND POLITICS

WHETHER they like it or not, doctors in the next few months will have to take an interest in politics. If they are to form an opinion on the coming white-paper which they will not later regret, they must study the evidence presented by the various official and unofficial bodies and so protect themselves from following blindly the enthusiastic exponents of this or that view. They are likely to be bombarded with memoranda, pamphlets and questionnaires and must be able to turn on each the cold scientific eye which they have learned to use on the advocates of a new drug or the inventors of a new syndrome.

Similarly they should be cautious in their approach to the public. The path of the propagandist is perilous, and the ease with which one may go rather too far along it is conveniently illustrated by a pamphlet lately issued by the Sheffield branch of the British Medical Association. In their anxiety to arouse public opinion the writers have probably misrepresented the Government's intentions, as the following extracts will show:

> Mr. Ernest Brown, the Minister of Health, has expressed a wish to place all medical services under *Local Government control*, which means in this City under the *control of the Town Hall*.
>
> * * *
>
> For your treatment you would have to visit a *Clinic*, and you would *have* to go to the Clinic in your own district. *You would have* NO CHOICE.
>
> The doctors in this Clinic would *not* be chosen by *you*, who alone knows the type of doctor you can trust. They would *not* be chosen by their own profession, who could at least assess their professional ability. *They would be chosen by a* LAY *committee*, who might be tempted to make these appointments with political ends in view.
>
> You might like *none* of the doctors in your own Clinic, but even if you do, the doctor you prefer might be "off duty," in which case you would have to see *any doctor who might be present.* Thus you might see a different doctor every visit. In other words, YOU WOULD HAVE NO FREE CHOICE OF DOCTOR, *and the doctor would be unable to choose his own patient, however incompatible the two might be.*
>
> If *you* were dissatisfied with your treatment, you would be unable to change your doctor as at present. Perhaps you could report an inefficient doctor, but *illness is urgent*, and meanwhile you would have to put up with inefficient treatment while your complaint was investigated by the usual bureaucratic machinery of committees, etc. In the meantime the patient might become crippled for life, or even worse, and you would be unable to go elsewhere for treatment.

From this the reader might suppose—is intended to suppose—that the Government set no store by free choice of doctor. Yet in their public statements several Ministers have gone out of their way to commend this principle:

> "Some people," said Mr. BROWN on March 26, "are afraid of an organised national health service, because they think it will inevitably be a soulless bureaucratic machine, by which patients will be dragooned into health and doctors dragooned into mediocrity and servility. If I believed that a service conceived in these terms was anything but an unreal bogy, I should myself be the first to condemn it, and I should shrink from the task of preparing for it. But I do not believe that an organised service must inevitably involve loss of personal or professional freedom. Health is an intensely personal matter and any national health service must be an intensely personal service. The family doctor, chosen by the family as their doctor, as the doctor in whom they have confidence and whom they often hold in real affection—this ideal must be the foundation stone of our service, and I am sure that it can be."

In the Commons debate on the Beveridge report Sir JOHN ANDERSON spoke of maintaining to the greatest possible extent the principles of free choice of doctor and of the family-doctor relationship as the background of general medical practice.

A pessimist has said that it takes a tank to fight a tank, and a fascist to fight a fascist: an enemy can be beaten only with his own weapons. The Sheffield branch, to justify their statement, might argue likewise that politicians must be fought with politics. But even in political warfare a high level can be maintained; and so far, in speeches on reconstruction of the medical services, no Minister has done less than justice to the plans of professional bodies. As people who claim the status of scientific workers, and have enjoyed scientific training, have we not a duty to apply scientific standards, so far as we can, to our political relations? Ought we not, indeed, to become a shining example to our fellow citizens? The difficulties are obvious, but so is the need.

ANTICOAGULANTS IN SURGERY

THE production of purified heparin and the synthesis of 'Dicumarol' have made it possible to exercise some control over blood-clotting. These two substances differ in their mode and duration of action, but both render blood less coagulable. Heparin has an immediate though somewhat transient effect, chiefly by inhibiting thrombin formation; the action of dicumarol, whether it is given by mouth or intravenously, does not begin for 24–72 hours but lasts a long time, and it probably depends on the diminution of prothrombin. There is a wide individual variation in tolerance to both substances, so that the effect of a certain dose cannot be accurately foreseen, and dosage has to be controlled by estimations respectively of coagulation or prothrombin times.

So far the main application of heparin has been in the prevention of postoperative thrombophlebitis and embolic complications, and in vascular surgery, but its scope may be far wider; thus D'ALESSANDRO [1] mentions its use in mesenteric, coronary and cerebral thrombosis. Its mode of administration and cost are drawbacks to its extended use. Heparin must be given intravascularly, the methods available being continuous, intermittent and regional; the regional method—direct injection into an artery exposed at operation—is used only in vascular surgery. The other two methods depend on intravenous injection, the continuous method being more widely practised in the New World and the intermittent in the Old. Since heparin is rapidly eliminated from the blood the continuous method seems more rational, but DE TAKATS [2] has found that even when a close watch is kept on the rate of flow it does not prevent fluctuations in the coagulation time; the disadvantage of undue immobilisation of the patient can be overcome with an apparatus which enables him to carry the saline flask, &c. about with him. The intermittent

1. D'Alessandro, A. J. *Surg. Gynec. Obstet.* 1942, **74** (int. abst. p. 62).
2. De Takats, G. *Ibid*, 1943, **77**, 31.

method involves injections every 4–6 hours, and it is important to use a fine needle to preserve the vein for subsequent injections and minimise the risk of hæmorrhage. With regard to dosage some confusion has arisen through the different units of measurement, and because the potency of heparin varies with the animal from which it is extracted. The National Institute for Medical Research has adopted the Toronto unit. The Connaught Laboratories of Toronto supply a solution containing 10,000 units (about 100 mg.) of heparin per 10 c.cm. rubber-stoppered vial. For continuous administration 1 c.cm. of this solution is added to 100 c.cm. of sterile physiological saline, and this is given by intravenous drip at a rate which will keep the clotting time at somewhere about two or three times the normal figure. As a rule 20–30 c.cm. of solution is needed daily. DE TAKATS has met with such wide variation in response to heparin that he gives a test dose of 1 c.cm. of this solution as a preliminary to heparinisation and makes a rough estimation of coagulation time at 10, 20, 30 and 40 min. after the injection, using a method simple enough, he says, for the student nurse. In his series hyporeactors were common among post-operative patients, and about 1 in 10 cases showed a hyperreaction.

The large series reported by MURRAY [3] in Canada and by BAUER [4] and HELLSTEN [5] in Sweden leave little doubt that heparin will much reduce the incidence of clotting complications after operation. Expense prohibits its use as a routine, but the Swedish workers maintain that by the use of venography to confirm the diagnosis in the earliest stages it is safe to confine heparin treatment to established cases, and that these will not amount to more than 2% of the patients admitted to a general hospital. At Mariestad Hospital it is the practice to do a venography—introducing a contrast medium into the deep veins of the leg and thigh and studying the vein shadows radiographically—in all cases with clinical signs suggesting thrombosis, and in this way about a quarter of suspected cases are eliminated. Unfortunately the interpretation of these X rays is difficult, and the clinical diagnosis of early thrombophlebitis is not easy. There may be merely an inexplicable rise in temperature or pulse-rate with some malaise, or pain in the calf or front of the thigh, often described by the patient and nurse as cramp. The skin may be discoloured—red, blue or bluish-white—sometimes in a marble pattern. A little œdema may appear behind the internal malleolus, and if both limbs are exposed for 10 minutes the affected one may not cool down like the other. There may be a local doughy thickening of the muscles, best felt when they are relaxed, and typically a tenderness along the course of the affected veins. But these signs are too vague to be always reliable. The experienced surgeon will recognise the patient who is specially liable to thrombosis—the fat plethoric type, or the woman who needs a difficult hysterectomy or other pelvic operation. It is here that dicumarol may prove valuable, for it has the advantages of constant composition and of being effective when given by mouth; even a single dose will prolong the prothrombin and coagulation times for 2–3 weeks. It has not yet been much used in this country, but the results reported from the Mayo Clinic are encouraging. ALLEN [6] and his colleagues divided 497 patients into five groups—those who had had an episode of pulmonary embolism or infarction after operation and survived, those with postoperative thrombosis, those who had had post-operative thrombophlebitis or embolism complicating a previous operation, those who had undergone abdominal hysterectomy, and those who had undergone various operations and presented such conditions as obesity, anæmia, neoplastic disease or varicose veins, regarded as increasing their liability to thrombotic complications. Dicumarol was given to these patients in 100 mg. capsules. The entire amount for each day was given in a single dose in the afternoon, that for the first day being 300 mg., and on subsequent days about 200 mg. The prothrombin time was determined daily after the third day, and the dosage regulated accordingly. In 477 cases a satisfactory increase in prothrombin time to 35–60 seconds (normal 18–22 seconds) was obtained. Thrombosis or embolism developed in only 4 cases out of the entire series of 497 patients receiving dicumarol, a figure far below the probable incidence. Two patients in each of groups 1 and 2 were affected, but in three of these the complication only developed when the prothrombin time had been allowed to fall below the desired level.

It is not possible to assess the value of dicumarol on this series alone. As DE BAKEY [7] points out, the prophylactic value of any anticoagulant is difficult to establish in such an unpredictable condition as intravascular thrombosis. Moreover, although apparently free from objectionable effects in most of the cases quoted, hæmorrhages were recorded in 31 cases by the Mayo investigators. In 24 cases the bleeding came from the operation site, while in others it came from the gastro-intestinal and urinary tracts. This bleeding tendency is unaffected by vitamin K, but fortunately can be arrested by transfusion of fresh blood, which restores the prothrombin; stored blood is less effective owing to loss of prothrombin. Contra-indications to dicumarol, according to ALLEN and his colleagues, are renal insufficiency, purpura of any type, blood dyscrasia with a tendency to bleed, existing prothrombin deficiency, and subacute bacterial endocarditis—in general, when there is any evidence of widespread infective embolic lesions anticoagulation therapy is unsuitable. When dealing with a manifestly infective postoperative thrombophlebitis, proximal venous ligation when feasible is a more certain method of avoiding embolism. It may be possible to combine the anticoagulants so as to employ them to their maximum advantage. Thus in vascular surgery, where prevention of early thrombosis is all-important, heparin must be relied on for the first 3 days, but dicumarol can be begun simultaneously so that this will take over the control of coagulation when its latent period of 2–3 days has elapsed. Similarly in the treatment of an existing thrombosis, whether venous or arterial, DE TAKATS

3. Murray, G. D. W. *Brit. J. Surg.* 1940, **27**, 567.
4. Bauer, G. *Acta chir. scand.* 1942, **86**, suppl. 74.
5. Hellsten, W. O. *Ibid*, suppl. 73.
6. Allen, E. V., Barker, N. W. and Waugh, J. M. *Proc. Mayo Clin.* 1943, **18**, 102, 107.
7. De Bakey, M. *Surgery*, 1943, **13**, 456.

gives heparin and dicumarol together in the first 3 days. He urges caution in the use of heparin, because hypersensitivity is not uncommon, and he is insistent that it is unsafe to give dicumarol without a daily determination of prothrombin level.

Annotations

TOWARDS BETTER SIGHT

THE University of Oxford is asking for £250,000 to found a department of ophthalmic research, and presents an excellent case for the appeal. Ophthalmology, in a practical way, has brightened the lives of millions; but the mere fact that it has done so much for so many has perhaps blinded us to its capacity to do more. Those who tend to regard it as a stabilised and static specialty will be disabused by the notes on Eyesight and National Health[1] which describe the Oxford project.

The objects proposed for research are the prevention of blindness, the improved treatment of eye disease, and the promotion of a higher standard of visual function throughout the land. The blindness following syphilis is preventable, though not entirely prevented, and on p. 334 Mr. Jameson Evans reports that ophthalmia neonatorum has been allowed to cause only one case of blindness in the Birmingham area in the last seven years. For detached retina research has already provided an operation "which gives, at the least, an even chance of restored vision." Many serious causes of defective sight, however, still await elucidation. Cataract and glaucoma, which account for some 70% of blindness in later life, cry out for further investigation, especially on the biochemical side. And was it inevitable that nearly a sixth of all children medically inspected in elementary schools in 1937 should have "defective vision and squint"? If so, how do we explain that (in 1938) the figure was 20% in London, but only 13·2% in the country? How far are eye defects—in Britain as well as in the tropics—preventable by sound nutrition? Hereditary blindness, the protection of eyes and eyesight in industry, and vision in the dark are other subjects demanding more attention. Again, experience in the RAF has proved the practical value of orthoptics, by which the eyes are trained to work together. "A comprehensive statistical research into the incidence of faults in binocular vision among the general population and an analysis of the results of treating such defects are needed. For instance, can people so treated discontinue wearing glasses? Probably many could. A psychological factor is sometimes present in spectacle wearers; certainly many more people wear glasses than really require them." In the study of important disorders such as migraine the ophthalmologist must maintain contact with psychologist, biochemist and internist; and all members of the profession must remember that the eye alone provides a window through which living processes can be studied.

Considering these facts even briefly, it is little wonder that Oxford should expect a good response, not only from employers of labour and from insurance companies, but from "all good citizens." The university already has the services of an accomplished investigator in Miss Ida Mann, FRCS, who is Margaret Ogilvie reader in ophthalmology. The new plan includes the erection and equipment of laboratories, lecture rooms, a library and a museum in connexion with the Oxford Eye Hospital when it is rebuilt at the end of the war, and the provision of salaries and working costs for full-time and part-time research-workers, teachers, and technicians. Even on a comparatively short view, it is doubtful whether money could be spent to better purpose.

[1] Issued by the Ophthalmological Research Endowment Committee. Secretary: Mrs. de Boisse, University Registry, Oxford.

PSYCHOLOGY OF THE REJECTED TABLET

OVER and over again we learn that medical discoveries are relatively useless unless they can be applied—unless the remedies or preventives can be brought to those who need them, and brought at the right time in the right form. Even when this is done, the complex activities of research-workers, manufacturing chemists, epidemiologists, quartermasters, pharmacists and clinicians may still be nullified because the patient—the proposed beneficiary—is not in the mood for medicine, or has somehow been set against it. A case in point is the difficulty of preventing disease in armies when the preventive is a regular dose of medicine. In his paper on p. 317, which is interesting and important for other reasons, Major Howie recalls that in the French Army in malarious countries any soldier could be required to furnish evidence that he had had his daily dose of quinine: "*pisses!*" said the sergeant; and if the Tanret test proved negative, the man was on a charge. This dramatic—and, as now appears, unjust—method has not been adopted for our troops, who today are given mepacrine ('Atebrin') instead of quinine; but something of the kind may be needed unless they can be persuaded to take their prophylactic more seriously.

The reasons for refusal are several. In the first place, the British soldier has long believed that any medicine administered to him when he is not sick can have one object only. In the last war, it was almost universally supposed that sergeants put Epsom salts in the tea, not with a view to promoting regular habits, but in order to reduce sexual potency. Such a belief would be laughable if it were no more than occasional. But prophylactic mepacrine seems to have revived it on a wide scale. (The belief is not confined to mepacrine, but also extends to prophylactic ascorbic acid.) Nor is this the only misapprehension about mepacrine: it is also said to be both dangerous and ineffective. The story of its toxicity appears to have arisen from a small outbreak of a non-malarial fever that happened to coincide in one unit with an initial course of the drug. This unlucky coincidence has enlarged itself, like an air-raid damage rumour, until the story now goes of an army prostrated by the tablets. The allegation of ineffectiveness is based, apparently, on the prejudices of the fabulous Colonel B; he is never tired of recounting how he has spent fifteen years in the tropics, and never a drop of these damned quinines has passed his lips; he's never had malaria, though he does admit a few sharp doses of fever. Faced with this barrage of myth and hypothesis, and the knowledge that malaria means for most people a couple of fairly pleasant weeks in hospital, what wonder that the soldier slips the tablet into a capacious cheek and later spits it into the wilderness of Tunisia.

This is clearly no simple problem for the doctor: it is a job for the educationist and the psychologist. The true facts about the values and dangers of mepacrine should be in the hand of every officer and man. In particular, the origins of the various rumours should be explained. And it should be made clear that malaria, even if not always dangerous to life, is not without its sequelæ, and that it is capable of delaying for long periods a campaign on whose ultimate outcome depends the speedy return of the troops home. Finally, if this is practicable, the dosage of mepacrine should be revised so that it is taken in a smaller quantity daily rather than four times a week. This would help to bring its administration into line with the thousand and one other bits of daily routine which are done with never a thought.

RECTAL FEEDS

MOST students, asked about the functions of the large intestine and rectum, would enumerate a little list with a confidence suggesting that the subject is a closed book. Yet within the last few years one or two of our classical ideas about these organs—that they excrete calcium and iron, for instance—have been proved wrong.[1] There is still a good deal of uncertainty as to what these parts of the alimentary canal should be expected to do. There was the bright idea that the rectum can absorb water selectively from sea-water, and that life-boats should be provided with Higginson syringes as well as oars and sails. The suggestion was a survivor—and a most unphysiological one—of the last war, but it needed a lot of controversy and experimental work to scotch it. This ultimately established that it could do a thirsty man no good to put sea-water into his rectum, and fortunately a practicable still has since been evolved.[2] The administration of "physiological" saline by rectum is of course a widespread practice, and 1–2 litres of water, with various salts, can be given daily in this way; but at one time it was customary to serve ambitious repasts in the rectum—eggs and wine were often incorporated into the so-called nutrient enema. This was given up largely because there was no conclusive evidence that the nutrients were absorbed, but the subject has been reopened by a study of the rectal absorption of glucose, salt and predigested protein. Mackenzie,[3] working with children in Glasgow, concludes that both the glucose and the peptones are absorbed, the glucose very irregularly, and salt almost as well as when it is given by mouth; but not all his evidence is convincing, and children may well differ from adults in this function. Alcohol, like other anæsthetics, is apparently well absorbed, but fats and undigested proteins are not, and may even be harmful because of the toxic substances formed by putrefactive bacteria. Neither will the rectum absorb enough amino-acids to maintain nitrogen equilibrium, and it seems better nowadays to give both them and glucose intravenously if the normal channels are unavailable, and to stop fiddling about with the rectum as an ersatz stomach. Nature designed the alimentary canal for one-way traffic, and it is wise to conform to such regulations.

PRETIBIAL FEVER

Daniels and Grennan,[4] of the US Army Medical Corps, describe an obscure febrile disease observed in 40 soldiers quartered near one another, between July 29 and Sept. 11, 1942. The relatively sudden onset was characterised by malaise, mild general aching, lumbar pain, severe frontal headache and postorbital pain. On the 1st or 2nd day mild respiratory manifestations (coryza, sore throat, cough) were complained of by 12 of the patients. In about 10 there was nausea and vomiting. Fever with recurrent chilliness or rigors persisted for 2–8 days, averaging 5·4 days, with a maximum of 99·8–105·6° F. Lumbar puncture was performed in 3 cases with stiffness of the neck accompanying the headache, but the cerebrospinal fluid showed nothing abnormal and no obvious relief of the headache followed the puncture. There was no decided enlargement of lymph-glands but the spleen was early palpable in nearly all cases and remained enlarged for from 5 days to over a fortnight. About the 4th day 24 of the cases developed an unusual symmetrical rash over their shins, consisting of raised, warm erythematous blotches with ill-defined borders, sometimes slightly tender to touch and sometimes vaguely resembling erythema nodosum; none of them were purpuric. In an additional 8 cases, besides the pretibial rash, a few lesions were scattered elsewhere. In 2 cases the rash became diffusely distributed over the entire body. In one case there was only a single lesion on the hand. No rash at all was found in 5 cases, otherwise typical. In a few cases the rash appeared to be urticarial. The cutaneous manifestations in most cases lasted only 2 days. The leucocyte count ranged from 2800 to 14,000 per c.mm., but leucopenia was present at some time during the acute illness in all except 5 cases; in 14 cases there was a slight terminal leucocytosis. Differential counts showed little deviation from the normal. Blood-cultures (done in all cases) were sterile, various agglutination tests were negative and malarial parasites and the spirillum of relapsing fever were not found. All the patients rapidly recovered without complications. A search for possible insect vectors led to no result. Inoculation experiments have so far failed and the cause of the disease remains obscure. An outbreak possibly of the same disease in about 35 cases in August, 1940, was described by Bowdoin.[5] A sporadic case, if observed in London during an influenza period, would most likely be labelled "influenza with a rash" or "atypical erythema nodosum," and these American observations may help to lessen the number of such headings.

BIOCHEMISTRY OF EFFORT SYNDROME

MANY efforts have been made to discover the somatic disorder in effort syndrome. Although neurotic inadequacy in the majority of these patients is well recognised, many doctors find it hard to account for the history of lifelong incapacity for effort otherwise than by supposing that there is some bodily inferiority, which may be qualified as constitutional, physiological, or psychosomatic.

One such explanation appeals to the phenomena of hyperventilation. Soley and Shock[6] concluded that "the respiratory alkalosis resulting from hyperventilation produces the symptoms of effort syndrome." Guttmann and Jones[7] could not confirm this view, but Quinn[8] adheres to it and suggests that, along with psychiatric treatment, rebreathing or holding the breath should be employed when the patient has symptoms of hyperventilation; he even advocates the administration of ammonium chloride to keep the blood pH at such a level that alkalosis will not result even though the patient over-breathes. Quinn, however, produces no fresh evidence, and the thesis he supports cannot be taken as proved, or even plausible. Master,[9] who has lately examined 30 naval patients with effort syndrome, which had mostly developed while the men were in training, found that they had small hearts on X-ray examination, and yielded an electrocardiogram showing a small QRS–1 and tall QRS–2 and 3 with occasionally a tendency to a right axis-deviation. In other patients with effort syndrome he found changes in the electrocardiogram after exercise which he interpreted as indicating inadequate blood-supply to the heart muscle. On rather slender evidence Master concludes that men of asthenic physique who have had symptoms of neurocirculatory asthenia before enlistment possess a constitutionally small heart which does not eject enough blood per minute to nourish the heart, skeletal muscles and organs of the body adequately in response to effort.

There is a striking contrast between the conclusions of such writers and those arrived at by Jones and Scarisbrick, reported elsewhere in this issue. When the latter required patients who had a history of almost lifelong effort intolerance, without conspicuous emotional dis-

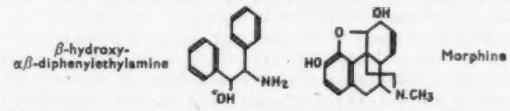
1. Nicolayson, R. *Skand. Arch. Physiol.* 1935, **72**, 126. Welch, C. S., Wakefield, E. G. and Adams, M. *Arch. intern. Med.* 1937, **59**, 1095.
2. See *Lancet*, May 22, 1943, p. 667.
3. Mackenzie, J. W. A. *Arch. Dis. Childh.* 1943, **18**, 22.
4. Daniels, W. B. and Grennan, H. A. *J. Amer. med. Ass.* 1943, **122**, 361.
5. Bowdoin, C. D. *J. med. Ass. Ga.* 1942, **31**, 437.
6. Soley, M. H. and Shock, N. W. *Amer. J. med. Sci.* 1938, **196**, 40.
7. Guttmann, E. and Jones M. *Brit. med. J.* 1940, ii, 736.
8. Quinn, R. W. *U.S. Nav. Med. Bull.* 1943, **41**, 769.
9. Master, A. M. *Ibid*, p. 666.

turbance, to carry out exercise, the fatigue which developed could not be attributed to respiratory alkalosis, though there might in some be a fall in the bicarbonate level following the production of lactic acid. The level of lactic acid reached in these experiments lent no support to the view that patients with effort syndrome behave otherwise in physiological respects than other people. There is much evidence that average young men will desist from muscular effort because of exhaustion when the level of lactic acid in the blood has risen to approximately 100 mg. per 100 c.cm., though older men desist earlier, and trained athletes only when the lactate has reached a higher level. Although in one or two instances Jones and Scarisbrick have observed a high lactate rise and a considerable fall in pH after relatively slight effort, none of the patients in the series they have recently examined exhibited this; yet they commonly desisted from effort while their lactate level was still low. It seems therefore that a psychological rather than a physiological anomaly has been demonstrated; the patient's bodily response to exercise does not differ in any discoverable respect from that of other subjects of his own age, but he gives up work much earlier than they would. It is unfortunate that the estimation of lactate in the blood, which affords so useful an indication of whether the man is at the point of maximal effort, is so technically difficult and delicate a procedure that it cannot be utilised more widely as an indirect measure of deficient endurance.

MORPHINE SUBSTITUTES

FOR many years now attempts have been made to synthesise substances with the properties of morphine, that most valuable drug without whose help, as Sydenham remarked, few would be sufficiently hard-hearted to practise medicine. In particular, the aim has been to make substances which will be free of the most serious objection to morphine—addiction—and much valuable work has been carried out on this subject under the auspices of the American National Committee on Drug Addiction. One of the difficulties in such work is that no really satisfactory experimental test exists for evaluating the effects of substances on the types of severe pain met with in disease. Ultimately the clinical test must be relied on for determining this, the most important action, though there are other actions of morphine with which new compounds can be compared experimentally. More evidence for and against pethidine has accumulated since it was summarised in these columns on May 8, and Batterman and Himmelsbach[1] have compared its status with that of morphine. This drug, first synthesised by Eisleb and Schaumann[2] in 1939, has three main types of action—analgesia, spasmolysis, probably dependent on its similarity in chemical structure to atropine, and sedation. It is more effective in the relief of visceral pain (e.g., from the peritoneum, pleura, smooth muscle) than of pain arising from skeletal and neurological structures. In postoperative patients it is, according to Batterman and Mulholland[3] more suitable than morphine, since it does not produce constipation. When used repeatedly in the control of chronic pain tolerance develops rapidly, as is the case, of course, with morphine. Pethidine can produce addiction even to the extent of physical dependence, so that on discontinuation of the drug an abstinence syndrome consisting of characteristic signs and symptoms develops, but it seems that addiction is unlikely to occur if therapeutic requirements are not exceeded. Batterman and Himmelsbach suggest that not more than 150 mg. every 3 hours should be given if habituation and undue cerebral irritability are to be avoided. A higher dosage may have no greater therapeutic effect and may have serious consequences. In pain due to spasm of smooth muscle pethidine may give dramatic relief. This applies not only to the intestine but also to other smooth muscle. Thus, Climenko and Berg[4] have demonstrated an antispasmodic action on the intact ureter, which probably explains the value of the drug in renal and ureteral colic. It has, on the other hand, the advantage of not inhibiting the contraction of the pregnant human uterus, even in large doses.

American investigators have approached the problem of morphine substitutes by the production of morphine



derivatives or of synthetic phenanthrene or carbazole analogues, but Dodds and his co-workers[5] have set out to produce simpler compounds of the diphenylethylamine series, having in chemical constitution the same kind of relation to morphine as the synthetic œstrogens of the stilbene series have to œstradiol. Preliminary clinical tests suggest that progress has been made. The most active compound, of which the formula is shown here with that of morphine, relieved pain when given by mouth in doses of 50–400 mg. every 4 hours.

NEUTRON TREATMENT OF CANCER

The "medical cyclotron" at the Crocker Radiation Laboratory of the University of California is being applied to the treatment of cancer. Stone and Larkin[6] mention that the first cyclotron used for treatment produced a beam of deuterons with 8 million electron volts (Mev.) of energy; the one they used is a bigger edition completed in December, 1939, the energy being stepped up to 16 Mev. The deuterons thus energised are in turn used to produce neutrons and with the beam in question the maximum energy of the fast neutrons is 21 Mev. Between December, 1939, and September, 1941, 128 patients were treated; 8 of them did not complete the course. Most of the 120 patients were selected for this treatment after a considered opinion that they could not be cured by surgery or X rays. The malignant lesions were: tongue 18, prostate 18, skin and lip 13, breast 11, larynx and pyriform sinus 9, floor of mouth and alveolar ridge 13, stomach and intestine 9, buccal mucosa 5, brain 4, nasopharynx 3, parotid 3, œsophagus 2, miscellaneous 12. The general lines of technique were those employed in deep X-ray therapy when an immovable X-ray tube with a horizontal beam is used. The reactions to treatment were classified as mild, moderately severe, severe and improved. Nausea and general malaise were classed as moderately severe; they became so severe that the patients required supportive medication. Irradiation of the upper abdomen caused severe systemic reactions and diarrhœa in almost all cases. Of the 120 patients treated, 61 had died by October, 1941. Of this group, 31 had gross tumours at the time of death; 29 of the 41 patients who had cancer of the mouth or throat had persistent ulceration at the time of death. Stone and Larkin take a sober and detached view of the whole investigation. They say "While the statistics presented appear discouraging, the effect of neutrons on tumours has been such as to encourage further study in selected cases. It was demonstrated, both clinically and pathologically, that some cancers disappeared as a result of neutron therapy." It should be borne in mind that the patients were mostly beyond relief by other measures.

1. Batterman, R. C. and Himmelsbach, C. K. *J. Amer. med. Ass.* 1943, **122**, 222.
2. Eisleb, O. and Schaumann, O. *Disch. med. Wschr.* 1939, **65**, 967.
3. Batterman, R. C. and Mulholland, J. H. *Arch. Surg.* 1943, **46**, 404.
4. Climenko, D. R. and Berg, H. *J. Urol.* 1943, **49**, 255.
5. Dodds, E. C., Lawson, W. and Williams, C. *Nature, Lond.* 1943, **151**, 614.
6. Stone, R. S. and Larkin, J. C. jun. *Radiology*, 1942, **39**, 608.

Special Articles

EFFECT OF EXERCISE ON SOLDIERS WITH EFFORT INTOLERANCE

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POOR effort response and ready fatigue are among the most important symptoms shown by effort-syndrome patients and for this reason effort syndrome is of particular importance in war-time. During the last war many attempts were made to find a physiological explanation for the poor effort response but without any great success (Haldane et al. 1919, Meakins and Davies 1920, Meakins and Gunson 1917, Cotton et al. 1917, Drury 1920, Briggs 1920). More recently Soley and Shock (1938) have advanced the idea that respiratory alkalosis following hyperventilation is responsible for some of the symptoms, but apart from this the question of effort syndrome (ES) received relatively little attention in the period between the two wars. By the beginning of this war the emphasis had shifted to the psychological side (Jones and Lewis 1941). The interwar period however had brought a great increase in our knowledge of the physiology of exercise, and it was considered of interest to investigate again the physiological response of ES patients to exercise.

The type of physiological response to exercise most fully understood is the response to short periods of heavy work in which the muscular demands far exceed the body capacity of supply and there develops an oxygen debt, partly shown by increased tissue- and blood-lactate, and a rising acidity shown by a falling blood pH. These represent for us a picture of physiological distress and partly account for the feeling of fatigue associated with such efforts. We have attempted to exercise ES patients and control subjects to the point of exhaustion in a short time and to compare the response of the two groups as shown by the blood lactic-acid and pH changes. It was found that ES patients would not attempt very heavy work, so it was necessary to use comparatively light work (6750 ft. lb. per min.); in order to exhaust the controls work for them was increased in severity after 10 minutes.

The present study also afforded us an opportunity to obtain some data about respiratory alkalosis and deficient arterial oxygen saturation in ES, both of which have been put forward as biochemical abnormalities responsible for the production of symptoms, including the fatigue felt in this condition.

MATERIAL AND TECHNIQUE

A group of 10 patients was chosen all of whom were free from organic disease and had ages ranging from 25 to 32. They all gave a history of effort intolerance from earliest recollection and it was felt that constitutional physical inferiority was more important in these men and had more to do with their excessive response to exertion than had emotional factors. We have already suggested a classification for ES patients which is particularly designed to evaluate the physical and emotional factors found in this material (Jones and Scarisbrick 1942).

A group of 16 controls was taken from the available hospital staff and included 7 doctors, none of whom took any regular exercise, 4 members of the physical training staff, and 5 others of whom 2 did a certain amount of track running.

Blood-samples were taken from the subject at rest, immediately after the cessation of exercise, to give the pH and lactate picture at the exhaustion point, and a third sample generally about 5 minutes later, to give the maximum lactate figure and also to determine the behaviour of carbon dioxide during recovery. The first and third samples were arterial blood taken from the femoral artery of each leg. The second sample was arterialised venous blood from the median basilic vein of the arm which had been heated to 45° C. in an arm-bath; this was done in preference to arterial puncture because the blood sample could be obtained without the slightest delay. Arterial punctures were not used in the controls as the physiology of exercise in normal people and in athletes has been extensively studied elsewhere and the results would not affect the conclusions to be drawn about ES. The blood, having been withdrawn in an all-glass syringe lubricated by the minimum amount of paraffin, was transferred under oil to a centrifuge tube and cooled in ice-water immediately. Samples were analysed for: oxygen capacity by the method of Sendroy (Peters and Van Slyke 1932); oxygen content and carbon dioxide content (Peters and Van Slyke); pH; and lactic acid content (Barker and Summerson 1941)

The ergometer consisted of a bicycle-chain wheel and pedals connected by the frame to the ground wheel which has a friction band with weights and a spring balance. The whole is supported by two uprights off the end of the bed so that the subject can pedal as he lies on the bed; though unorthodox the position was comfortable, and was used in order to facilitate the collection of blood when the subject reached his exhaustion point. The rate of pedalling, 42 revolutions per min., was set by a metronome which the subject could both see and hear. A trial run was always given the day before until the subject was familiar with the machine. The end point was taken when the subject, in spite of all encouragement, was no longer able to continue pedalling to the rate of the metronome.

It was found to be impossible to exhaust some of the control subjects within a reasonable time at the intensity of work used for the effort syndromes. In order to obtain an exhaustion end point, the intensity of work (6750 ft. lb. per min.) was raised at the end of 10 minutes by increments of 1700 ft. lb. per min. every minute until a level of 10,000 ft. lb. per min. was reached.

EXERCISE RESPONSE

All the patients performed less work than the least active of the control subjects. The times recorded for the patients range from 3 min. 10 sec. to 7 min. 15 sec., with a mean value of 5 min. 26 sec. Every control subject so far tested, both within and without this series, has been able to exceed this time.

This poor performance on the part of the patients may have its origin in a definite physiological inefficiency, or in an abnormal psychological attitude towards the work, resulting in a reluctance to persevere. The conditions of the experiment were chosen so that physiological difficulty would show in most cases as a rising body acidity and a large rise in blood lactic-acid. Gross physiological inefficiency would then be shown as the development of these signs of physiological distress as a result of the performance of a relatively small amount of work.

We have observed such inefficiency both in control subjects under certain conditions and in a few effort-syndrome patients.

One of our control subjects was normally able to work for 11¼ min. as a result of which his blood pH had moved from 7·40 to 7·22 and the lactic acid content of the blood had increased from 12·0 to 80·0 mg. per 100 c.cm. When he was tested in a post-infective state, immediately after influenza, he was able to work for only 4½ min. but showed changes of lactic acid and pH similar to those shown when he was in good health (pH 7·42–7·26, lactic acid 10·7–81·7 mg. per 100 c.cm.).

Exaggerated response to exercise, of this type, is occasionally found in effort syndrome; the following case is an example.

A man who has been discussed in a previous paper (Jones and Scarisbrick 1942) had had effort intolerance for only a few months before admission to hospital. There was no evidence of neurosis but he had a persistent tachycardia for which no cause could be found. He did not consider himself ill and had excellent morale. When tested on the ergometer he worked to complete exhaustion and shortly afterwards lost consciousness. He worked for only 4½ min. His blood lactic-acid rose from 11 to 110 mg. per 100 c.cm. and the pH fell from 7·4 to 7·1.

In both these cases the body was responding very inefficiently to the work, as shown by the high lactate rise and large pH shift for the small amount of work done. The patients in the series reported here, however, did not show this exaggerated and inefficient response. As a result of the exercise the lactic acid rose from a mean resting value of 11·7 mg. to a mean value of 47·9 mg. 5 min. after the conclusion of exercise (range 31·6 to 87·6

mg. per 100 c.cm., the latter figure being outstanding and raising the mean considerably). The corresponding changes in the control subjects were: resting 11·4 mg. rising to 80·9 mg. (range 40·7 to 118 mg.). The breakdown in the ES patients is clearly not due to overwhelming physiological distress.

Any study of maximal fatigue is made difficult by the fact that the point at which a person gives up is an arbitrary one depending on various factors including mood, incentive, persistence, &c. According to Knehr and his colleagues (1942) the average young man will stop work on a treadmill when the level of lactic acid in the blood has risen to approximately 100 mg. per 100 c.cm.; and for some time it has been felt that the level of blood lactate obtained after exercise gave an indication of the general persistence of the subject. It has been found however that this figure is influenced by age, which lowers it (Robinson 1938) and by training, which raises it (Knehr et al. 1942). Figures as high as 200 mg. have been obtained with trained athletes. The control subjects used here, with the exception of the PT staff and the 2 runners were in general untrained and rather older than the patients and with 3 exceptions attained a level of lactic acid in the blood of 70 mg. or over. The lactic-acid level in the patients at the conclusion of the exercise was much less than this (mean 47·9 mg.) with one exception (case 9). The most obvious conclusion to be drawn then is that the poor effort response in ES patients is due to lack of persistence.

Oxygen metabolism.—It has been suggested (Haldane et al. 1919, Hick et al. 1937) that deficient saturation of the arterial blood with oxygen occurs in ES patients as a result of the rapid shallow breathing which has been described in these cases, and these authors attribute the fatigue and certain other symptoms of ES to this anoxia. The 10 cases presented here did not show particularly rapid respiration at rest and showed no sign of deficient arterial oxygen saturation at rest. The oxygen saturation of the arterial blood in these 10 cases when at rest varied from 97% to 92% (mean 95·6%). The discrepancy between the two findings is in all probability due to the choice of cases. We have had the opportunity of studying several hundred cases of effort syndrome and of these only a very small percentage show the rapid shallow respiration described by Haldane and his colleagues (1919); such extreme cases may suffer from deficient oxygenation. Certainly, as is shown by the cases presented here, poor effort response and ready fatigue exists in effort syndrome cases without any trace of arterial oxygen unsaturation.

Further we have obtained figures for the oxygen saturation of blood at the conclusion of exercise ranging from 90 to 95% (case 6 is an exception; here the oxygen saturation was only 72%); when it is remembered that these figures were obtained from arterialised venous blood, and that in normal subjects there is a tendency for arterial saturation to fall during strenuous exercise, it seems fairly certain that deficient oxygen saturation cannot be held responsible for the fatigue in ES.

HYPERVENTILATION

Respiratory alkalosis occasioned by hyperventilation has been much discussed since Soley and Shock (1938) suggested that this was responsible for some of the symptoms of ES. Earlier work done here gave no support to their contentions (Guttman and Jones 1940). Reports on the subject have recently been reviewed by Wood (1941). Our present concern has been to see whether hyperventilation with development of alkalosis occurred as a result of exercise in the type of patient we have described. The results show clearly that though there may be a fall of carbon dioxide pressure after exercise this is not abnormal in amount (generally 3 or 4 mm. Hg, the most extreme being a fall from 40 to 31 mm. Hg) and is correlated with fall of bicarbonate following the production of lactic acid. In no case did the blood pH become more alkaline than the resting value.

It might be argued that we have looked for the development of alkalosis too soon. We were guided by the fact that in all the patients chosen, excessive respiration had almost died away 5 min. after the conclusion of exercise, and whenever we have taken another blood sample after a further 5 min. this has simply shown a slow return of the pH to the resting value.

We have not tried to show that hyperventilation alkalosis does not occur in ES patients as a result of exercise, for in some few patients it undoubtedly does, but that in this particular group of patients, respiratory alkalosis did not contribute to fatigue and that hyperventilation alkalosis must be regarded as accessory to the symptoms of ES.

DISCUSSION

The 10 patients chosen for this study show very poor response to exercise as judged by the amount of work done. At the same time, however, there is no major biochemical abnormality in their response. The pH and lactate were in keeping with the amount of work done, though we have occasionally seen a case where the rise of lactate and pH shift is excessive for a small output of work. The latter type of response might be expected in a patient with for example a congenital heart lesion, but in the case we have recorded there was no evidence of any organic disease. Such a case furnishes the best possible evidence of effort intolerance in that the poor work performance is accompanied by maximal changes in the level of blood lactate and change of pH. This is not true of the group of patients studied whose poor work performance was accompanied by a proportionately small rise of lactate and change of pH. They all claimed to have worked to exhaustion point and objectively they appeared distressed though not so seriously as the control group. These men had had effort intolerance since childhood and had not played strenuous games. They therefore were not in the habit of driving themselves to exhaustion point as does the average man who plays football. On the contrary they avoided violent exercise and in 3 cases this was determined by fear of possible physical damage resulting from over-exertion. We feel that this type of work experiment does give an index of the man's persistence in a setting of physical distress. In those cases where a really high level of lactate is obtained the test may also be said to give an indication of the man's physical proficiency. For instance, a man whose blood lactate rose to 90 mg. per 100 c.cm. but who only worked for 5 min. is obviously less fit than a man whose blood lactate reached the same figure after working for 10 min. We feel that some measure of persistence would be invaluable for studying the "unwilling soldier" but realise that the test outlined is technically too difficult for routine use. We are investigating the possibility of a significant correlation between the results of this test and various psychological tests of persistence.

In the patients studied deficient arterial oxygen saturation was not found at rest or as a result of exercise. Further there was no tendency to the development of a respiratory alkalosis after exercise though this does undoubtedly occur in some cases; such an abnormality however is incidental to the fundamental problem of poor effort response in ES.

SUMMARY

The effort response in 10 patients giving a lifelong history of effort intolerance and in 16 normal controls has been studied, using a bicycle ergometer.

The amount of work done before reaching complete exhaustion was considerably lower in the patients than in the controls.

The rise of lactate and fall of pH was considerably greater in the control group than in the patients.

In the patients no evidence of deficient arterial oxygen saturation was found either at rest or as the result of exercise.

In the patients there was no tendency to develop a respiratory alkalosis after exercise.

The value of this test as a measure of persistence in spite of physical distress is discussed.

We wish to thank Dr. W. S. Maclay, medical superintendent of this hospital, for permission to publish these cases. We also have pleasure in thanking Nurses J. Ascott, J. Eedle, B. Marler, E. Nicholls, and P. Tait for technical assistance, and Dr. R. Freudenberg for the loan of a potentiometer.

One of us (R. S.) is indebted to the Medical Research Council for a personal grant during the period of this investigation.

(*References at foot of opposite page*)

In England Now

A Running Commentary by Peripatetic Correspondents

ONE of my colleagues often grouses, but his popularity is undimmed for his grumbles are never personal to himself, and he expounds them entertainingly. He labels his complaints "divine discontent" which he says is the fit and proper attitude towards things which are wrong and could be put right. His latest theme is that far too many people are appointed to important and specialised jobs because they are good at something totally different. I must admit that having heard him expatiate on the point, his case has substance. He first reminded me of two professors in our old medical school. One was appointed to a science chair as a young man on account of brilliant research work, and although this was well sustained, he was unquestionably the worst teacher either of us ever heard. The other was appointed to a clinical chair because of his excellent lecturing style, and his clinical acumen turned out to be, shall we say, unimpressive. One finds many other examples of this principle of appointment, though admittedly they are not always unsatisfactory. A year or two ago, academic circles in America were set arguing fiercely by the election of one of the country's most brilliant chemists as president of a great university. That in this case the appointment was successful, and that the fingers which laid down the test-tube triumphantly took up the administrator's pen, proved only the great ability of the professor. Indeed, the extent to which the success of this appointment is quoted suggests that it is remarkable that a laboratory man could be so successful in so different a field.

Long before this war it was commonplace that, when a research man reached a certain degree of eminence whether in academic or industrial circles, more and more purely administrative work was forced on him. The exigencies of crisis and emergency made this ever more inescapable, for, scarce though research men are, they are commoner than highly skilled administrators. The first lesson from these observations seems to be that research ought to be more widely appreciated as a job in its own right, and not one to be carried out by someone who is distracted by managerial work in a firm or teaching routine classes. The other lesson is that there should be more appreciation of administration as such, and the sceptre of organising authority should not be thrust into the hands of a man because he is an honours graduate in classics or conchology or was a prefect at St. Winifred's and is a prominent member of the Drones Club.

* * *

The medical columnist is more shackled than his lay brother—he can't write: "Among the deformities at the Duchess's debutantes ball I noted . . .," or "Dining at Claridge's the other night I heard young Lord Mud telling one of his long myxœdematous stories, and recalled that his mother, the old Dowager, kept a splendid goitre . . ." Still we do our best. Last week I happened to be in our county mental hospital when they were doing their first leucotomy. The patient before the anæsthetic talked continuously: she was being poisoned in 24 different ways by a ginger nurse—give me a cigarette—who scratched her and bit her in 24 different places—give me a cigarette—in 24 different dresses, a long list of names, give me a cigarette; over and over again like a spoilt record. It was easy to see one of the reasons why she had been selected. The surgeon removed a ¾ in. disc from each parietal, divided the dura and went in with his leucotome. I don't know whether he was a bit of a water-diviner, but he tapped the ventricle from each side.

The prefrontal area is supposed to be connected with prevision, and merely watching the operation has stimulated mine. I have been seeing a long shelf full of *Medical Annuals*, stretching into the dusk of futurity. I keep taking them down and slitting the uncut pages with a leucotome. Ah, 1953—"Any good results that followed the old operation of leucotomy are now known to have been due to neuro-protein shock." H'm; skip a decade. Here's '63, only one reference: "Blitzkrieg postulates the generally accepted fact that leucotomy of *any* part of the brain gives equally good results in mental patients." H'mm, don't suppose it's mentioned in '73, which I can just reach and read, although it's in my second childhood. Yes, it is, one reference again, Soloni, the Italian alienist:

"The old operation of leucotomy may not have killed many patients, but it did definitely kill the 'centre' idea, which prevailed from Aristotle to the phrenologists and surgeons of the '40s. That the brain had definite 'centres,' each with its definite function, was the inevitable conclusion of shopkeepers and professional men in an ill-educated mechanistic age. They were not imaginative enough to grasp the universality of every part of the brain, its limitless capacity by reason of its limitless associations; so obviously they could not understand that when centres are formed as they are in many mental diseases, when nervous tracks are made and frequented as in paranoia, schizophrenia and the fixed cast-iron personalities, that in itself is a sign of degeneration; in other words impulses are conveyed along fixed paths because free communication between every cell and every cell is in some way hindered. If one falls back on the trite telephone metaphor, then a good telephone system with its exchanges, subexchanges, lines, numbers and subscribers is like a diseased brain, but in a healthy one every subscriber is in telepathic communication with every other subscriber at will. Moreover, an extension of cortical tissue in an animal's brain does not mean any new centres, but that each cortical cell has so many more new associates. It is obvious . . ."

* * *

Caramulo is a tiny village in the hills between Coimbra and Oporto. In 1918 there was nothing there but the village. Now there is an enormous TB sanatorium with accommodation for 800 patients. The whole place has grown up through the enterprise and management of Dr. Lacerda, who is still in charge. We arrived unexpectedly in the evening thinking we should find a hotel in the village, but as there wasn't one the director of the place and his staff showed us what Portuguese hospitality is like. We dined with Dr. Lacerda and a few of the staff at his private house, and appreciated both the sucking pig and his charming daughters' fluent English. I had an excellent room in the sanatorium and next morning got up early and escaped to the hills for a couple of hours. The dwarf crocuses were delightful. We spent most of the day in seeing over the sanatorium and its surroundings. The buildings are large and numerous. There is a resident physician for each, and specialist surgeons, radiologists and a dentist are attached to the place. The prices charged to patients range from 650 to 1900 E. a month, but a proportion are accommodated free. The buildings vary in age and in luxuriousness of fittings. One is set apart for patients from the army, another for patients from the railway services and the navy. Staff and patients lunch together, and they seemed to have no difficulty in fitting us in. We saw the table ware being sterilised after each meal, and were taken over the milk sterilising plant, the laundry and the sewage farm, the effluent from which does wonders for Dr. Lacerda's orange groves further down the hillside. The whole show is a good example of what conscientious and efficient private enterprise can achieve, and there is a great need for such a place in Portugal where the incidence of tubercle is high.

* * *

"Without disloyalty to my old school or my old college, I must admit that the bulk of my useful education has been

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culled from the backs of cigarette cards and the wonderful Penguin and Puffin series."

This statement was back-broadcast from the year AD 2000 by a Cabinet minister with an unusually high coefficient of honesty, and its reception by me was induced by reading *Butterflies in Britain* (Richard Chopping, Puffin Picture Books, pp. 31, 9*d*.). This folder—it is not much more—deals with about half the British butterflies and has over fifty vividly coloured plates. I can imagine no easier introduction to this fascinating subject, though I regret a sentence on page 10 which might bring the wrath of cabbage owners on the innocent head of the greenveined white, a demure and delightful creature. People often laugh at the "bug-hunter" with his net and his smells of cyanide and camphor, and I think quite rightly, for he kills the thing he should love and his mind often never gets past the amor habendi in the cabinet drawer. But he who studies and respects them in the life—after all most of them were on these islands long before we were—like all who marvel at natural mysteries finds himself in a land of great peace. The modern youth's craving for mechanism is driven by a variant of the power motive and is a sorry tranquilliser, but he who studies nature enters into an old heritage and has the universe for his schoolroom. For a good naturalist not only delights in the mysteries of atomic structure and stellar spectra but will get as much content from watching a cloud of flies, the sexual eccentricities of the short-palped cranefly, as from spotting the ductless glands that dictated a Prime Minister's speech or the motive structure of an Archbishop's sermon.

* * *

Office work in London is a sad error of pseudo-civilisation; like Mark Twain's brigand I cannot realise that I have only to open the window to get out.

Public Health

REGIONAL TREATMENT OF OPHTHALMIA NEONATORUM

P. JAMESON EVANS, M D CAMB, F R C S, DOMS
ASSISTANT SURGEON TO BIRMINGHAM AND MIDLAND EYE HOSPITAL

IN the past two years the increase in venereal disease has reached such proportions that a policy of publicity has been forced upon the Government, and this has been supplemented by regulation 33 B. At the recent meeting of the Blind Association of Great Britain concern was voiced at the rising number of blind babies afflicted with venereal disease, and in particular of those blinded through the complications of ophthalmia neonatorum. It is remarkable, therefore, that no such increase has occurred in the Birmingham area, and it may be of value to record the methods used in this city, to support the suggestion that an increase of blindness from ophthalmia neonatorum is preventable, even under war conditions.

The story of ophthalmia neonatorum in the past forty years is a striking record of preventive achievement. In 1901 Bishop Harman noted that cases of blindness caused by ophthalmia neonatorum in the London County Council children formed 36% of the total, and this high proportion was probably present in the rest of the country too. The reduction in the number of children blinded by this cause is an example of excellent coöperation between the voluntary medical services and the public health authorities, and has been attained by a combination of administrative and therapeutic measures. The present incidence of blindness from ophthalmia neonatorum in the Birmingham area is extremely small: in the last seven years there has been only one case, in a population of 1¼ million.

DEVELOPMENT OF PREVENTIVE MEASURES

The first step towards improvement was taken in 1925, when the incidence of ophthalmia neonatorum was still very high, and the resulting blindness was not uncommon. Before that time the notification and treatment of cases was left largely to the discretion and ability of individual doctors and midwives, but in 1926 such a serious position had arisen that a meeting was called between the public health authorities and the committee of the Birmingham and Midland Eye Hospital, and it was arranged to concentrate the notification and treatment of all such cases, as far as possible, at the Birmingham and Midland Eye Hospital. Henceforth all midwives under the jurisdiction of the city public health department were obliged, and many nearby but beyond its authority were encouraged, to send all cases of purulent ocular discharge in infants to the hospital. Since then two notable results have been achieved—the city of Birmingham has by far the highest rate of ophthalmia neonatorum notification in the country, and it has the lowest rate of infantile blindness from this cause. These two facts are cause and effect.

The public health department gave financial assistance towards the maintenance of a ward at the hospital reserved for ophthalmia neonatorum, with provision for both babies and their mothers, and a nursing staff with specialised experience and skill. The treatment at that time was mainly after Credé's method, and demanded frequent saline irrigations. These involved a considerable degree of manipulation of the eye, with eversion of the lids, and could only be successfully undertaken without damage to the eye by those possessing a light and experienced touch. Even so, the results were not uniformly good, so that the number of eyes severely damaged in 1936–38 was ten, and in 1940–42 was four. Treatment with sulphapyridine has been standard since 1939.

Further extension of the nursing facilities for treatment was again provided in 1930, by joint arrangement between the public health department and the Birmingham and Midland Eye Hospital, when a system of home visiting by qualified ophthalmic-trained nurses was instituted; this has continued throughout the war years, and shows no diminution in value or demand. By this means control is obtained of the home environment, treatment is ensured at regular and frequent intervals, and the doubtful efficiency of the mother is eliminated. Between 2200 and 2500 home visits are paid annually by a special nursing staff (see table), and unsatisfactory cases are immediately referred back to the ophthalmic surgeon. Under the present war conditions in an industrial area, where many women are at work in factories and unable to give enough time to their children, the value of home visiting is greatly enhanced, and this is a potent factor in the maintenance of a low incidence of blindness in the city.

Year	Total notifications in B'ham	Treatments given	Home visits	Gon.-pos.	Complications
1938	1085	3138	2436	17	3
1939	995	4082	2395	11	?
1940	1039	3930	2388	7	1
1941	961	4209	2337	8	1
1942	1226	5914	2227	15	2

Home visits began in May, 1930.

SYSTEM NOW IN FORCE IN BIRMINGHAM

Any midwife in the city area having under her care an infant with a discharging eye, in which discharge has begun within three weeks of birth, is now required to send it to the Birmingham and Midland Eye Hospital. The age of the infant need not necessarily be within the three weeks defined by the public health regulations, and older infants are also freely referred for advice and treatment both by midwives and by medical officers of child-welfare centres.

At the hospital the infant is examined by a doctor, and a smear and culture are taken for pathological examination in all cases showing any discharge whatever, irrespective of the severity of the ocular condition. By this means many severe cases are seen, diagnosed and treated in their earliest stage, and often the condition is checked before serious damage can occur. Immediate pathological confirmation is of great value also in the recognition of cases likely to become severe, and in governing the advisability of admission. All positive gonococcal cases are admitted and also a number of cases showing streptococcal or other virulent cultures—of notified cases, only 1% in the past five years has been of gonococcal origin.

	1936	1937	1938	1940	1941	1942
Admitted	96	62	80	27	15	17
Gon.-positive	8	7	17	7	8	15
Impaired eyes (gon.)	2	1	2	0	0	0
Impaired eyes (non-gon.)	1	1	3	1	1	2

Before 1938 the routine treatment was a modified form of Credé's method, but silver nitrate was used as a rule in weaker strength than 1%, and emphasis was laid on the regular washing of pus from the conjunctiva and cornea by warm saline. In severe cases irrigation was sometimes necessary two-hourly day and night, imposing a severe strain both on infant and nurses, and demanding the utmost care in manipulation. Fortunately, this exacting treatment is now seldom necessary, and certainly not for the long periods, sometimes of weeks, which were once the rule. Since August, 1938, sulphapyridine has been a routine measure—¼ of a tablet (0·125 g.) every six hours in the milk—and has proved uniformly successful, except in a few cases of obscure but not gonococcal origin, associated with marasmus. With this drug, most gonococcal cases are free of discharge within four or five days, and no cases of recurrence have been encountered. This treatment has reduced corneal ulceration both by the early removal of infected pus from the conjunctiva and cornea, and also by the elimination of frequent manipulations of the lids, which even in the most skilled hands were a constant danger to the œdematous corneal epithelium. Irrigation is still required on admission, but it is now relatively harmless.

Usually sulphapyridine is given for two days, and if the eyes are not clear of discharge sulphathiazole is then substituted; the latter drug agrees with most infants better than sulphapyridine. Under this treatment almost all cases show rapid and complete recovery, but some cases growing staphylococci of the flavus group are still resistant to treatment.

* * *

It can be said, therefore, that in the Birmingham area ophthalmia neonatorum is under control, and that no increase in infantile blindness from this cause has been noted since the war. Such a satisfactory state has resulted from the efficient preventive treatment adopted both for mother and child, the antenatal supervision of mothers, the concentration of treatment in a single centre where specially skilled nursing is available, and the early notification and treatment of all cases within the defined terms of the disease.

My thanks are due to Dr. E. W. Assinder, pathologist to the Birmingham and Midland Eye Hospital, for help in preparing this paper.

FROM THE ANNUAL REPORTS

The reports of MOHs for 1942 are in general uninteresting, for circumstances did not permit the exploration of matters which were not of immediate bearing upon the health of communities and the year did not present many features of outstanding importance. But there are exceptions.

Dr. D. M. CONNAN (Bermondsey) reports a prosecution for the sale of curry powder containing 44 parts per million of lead. The summons against the retailer was dismissed on the defence of warranty and that against the manufacturer on the defence that in present circumstances "the presence of extraneous matter was an unavoidable consequence of the process of collection." No-one can question the legality of the decisions, but if the object of the law is to protect the consumer it may be remarked that he will suffer just as much from lead legally present in his food as from that illegally introduced.

Dr. A. B. WILLIAMSON (Portsmouth) makes two important comments. The first is connected with a decline in tuberculosis mortality from the high rate of 1941, though the rate is still higher than in the immediate prewar period. "The increase," he says "is undoubtedly due to (*a*) lowered resistance from anxiety, fatigue and overwork, and difficulty in maintaining desirable standards of environment, and to (*b*) increased liability to infection from overcrowding, bad ventilation resulting from blackout, and infection from unpasteurised milk-supplies." Except the last, these adverse conditions would be much the same in 1942 as they were in 1941 and we should expect the results of continued adverse conditions to be progressive, unless there were some opposing favourable factors to neutralise those which are adverse. The rise in tuberculosis in the last war proved to be temporary and when it was over in 1919 the decrease in the disease was resumed despite social conditions which were by no means favourable. Possibly the chief element in causing increased mortality in the two wars is lowered resistance due to anxiety in those with present lesions which will either advance or recede according to environmental stresses. If this is so, mortality would tend to fall after a rise in any circumstances.

The second comment is on the temporary suspension of slaughterhouses. "It is earnestly hoped, therefore, that after the war there will be no return to the old insanitary medieval conditions. . . ." We have all had this hope since Ward Richardson's day—and have been disappointed for half a century; and now the war offers opportunity to convert the hope into a demand. Amid the stress of so much to be done when the war is over let us not overlook this matter of slaughterhouses.

While cerebrospinal fever continued to decline throughout 1942, the two chief virus infections of the nervous system were at a very low level; making allowance for the steady improvement in reporting cases, poliomyelitis was probably rarer in 1942 than in any year since it was made notifiable, and new cases of encephalitis lethargica could be numbered on the fingers. For many years deaths from this disease have outnumbered notifications, and now these too are declining, as the damaged relics of the epidemic which peaked in 1923 pass out of existence. Cases of encephalitis occurring in the course of the common virus diseases (measles, chickenpox, &c.) were as rare as ever; the anxieties of the war have not, it seems, made the nervous system more vulnerable to infection. In Manchester, with a population of over three-quarters of a million, 20 deaths from CSF, 1 from polio, and 15 from "acute infectious encephalitis" were registered in 1942. There were 120 notifications of CSF, but Dr. METCALFE BROWN gives no information on notifications of the two other diseases. In no 1942 report as yet received is there special mention of polio or sleepy sickness.

Infectious Disease in England and Wales

WEEK ENDED AUG. 28

Notifications.—The following cases of infectious disease were notified during the week: smallpox, 0; scarlet fever, 1890; whooping-cough, 1915; diphtheria, 614; paratyphoid, 7; typhoid, 16; measles (excluding rubella), 986; pneumonia (primary or influenzal), 337; puerperal pyrexia, 126; cerebrospinal fever, 48; poliomyelitis, 14; polio-encephalitis, 2; encephalitis lethargica, 0; dysentery, 129; ophthalmia neonatorum, 130. No case of cholera, plague or typhus fever was notified during the week.

The number of civilian and service sick in the Infectious Hospitals of the London County Council on Aug. 25 was 1497. During the previous week the following cases were admitted: scarlet fever, 179; diphtheria, 38; measles, 23; whooping-cough, 41.

Deaths.—In 126 great towns there were no deaths from measles or scarlet fever, 1 (0) deaths from an enteric fever, 6 (0) from whooping-cough, 10 (0) from diphtheria, 64 (2) from diarrhœa and enteritis under two years, and 7 (1) from influenza. The figures in parentheses are those for London itself.

Wallasey reported the fatal case of an enteric fever. Manchester had 7 deaths from diarrhœa, Liverpool and Birmingham each 6.

The number of stillbirths notified during the week was 184 (corresponding to a rate of 30 per thousand total births), including 12 in London.

PROTECTING THE X-RAY WORKER.—Last November the Minister of Health arranged for the National Physical Laboratory to assess the amount of radiation received by X-ray workers in the course of their employment. The test is made by means of a dental film which the worker carries in his breast pocket for a day. It is developed and the tint compared with a colour series corresponding to known doses of radiation. The Minister is anxious that this test should be made every three months and he is disturbed to learn that only a few hospitals have so far made a second application for films.

Letters to the Editor

SWABBING OF CONTACTS IN DIPHTHERIA

SIR,—The memorandum on diphtheria published in your issue of July 3 embodied the experience of medical superintendents of London and provincial fever hospitals, bacteriologists and public-health administrators. Its chief aim was the promotion of a more rational approach to the problems of investigation, disposal and treatment of diphtheria and doubtful diphtheria. It discussed also a possible method of overcoming the present rigid system of notification which makes the published incidence figures entirely fallacious—an important matter in its relation to immunisation. In the space available no attempt was made to offer detailed advice on the control of diphtheria outbreaks but there was a definite plea for discrimination in swabbing contacts of a diphtheria case. Questions on this have been raised in letters from eight pathologists (*Lancet*, July 17) and Dr. A. W. Downie (Aug. 7) who also dispute the statement that "the child with a healthy throat and nose is not likely to harbour the KLB for more than a brief period, and, in the absence of catarrhal conditions, is not likely to disseminate diphtheria." Large-scale investigation of diphtheria has shown that individuals with healthy mucous menbranes eliminate the organism rapidly. The importance of an unhealthy mucous membrane in maintaining the carrier state is emphasised, for example, time and time again in successive MAB and LCC annual reports from 1926 onwards: the introduction of tellurite medium did not alter the fundamental truth of this observation. It is a commonplace experience in fever hospitals that healthy contact carriers revealed by swabbing have become free from infection by the time they are admitted to hospital. But even healthy carriers can be reinfected, particularly if they are treated in open diphtheria wards, as has often been demonstrated by a change in the type of organism. This factor must be taken into account in assessing the duration of any carrier state.

In the bacteriological investigation of a diphtheria outbreak a definite pattern is revealed, its intricacy depending on many factors. If circumstances are favourable to the organism, it may create many clinical cases but even more carriers. The carrier pattern is not static: early contacts, who may occasionally transmit infection in the interval, will often rid themselves of infection before any investigation could be undertaken, and other carriers will have taken their place for a short or long period. Routine swabbing may demonstrate a phase of this changing pattern, but it is wrong to assume that carriers revealed are necessarily playing any part in the outbreak other than as transient victims. The carrier with an abnormal nasopharyngeal mucosa is a much more potent source of infection, because he is likely to be persistent and to produce a heavily contaminated droplet spray. In outbreaks of diphtheria definitely traceable to a carrier the originator has in fact often been suspected first on clinical grounds—usually because of an unhealthy condition in the nose. Dr. Turton (*Lancet*, Aug. 21) upholds routine swabbing, but admits that a number (unspecified) of the 19 carriers found among 2176 children examined were only cleared after tonsillectomy. We would suggest that the work involved in swabbing this number of children was out of all proportion to the results achieved, and that had he acted on the lines laid down in the memorandum he would have found the probable causes much more easily.

Dr. Downie cites a small diphtheria outbreak in which 5 carriers were revealed by routine swabbing of contacts. He implies that their subsequent removal to hospital was responsible for bringing the outbreak to an end, but this is surely doubtful since 8 clinical cases had already occurred in the community of 24 persons, of whom 5 were shown to be immune. Every public-health administrator has experienced similar outbreaks which terminated on recognition and isolation of clinical cases without any swabbing of contacts. It is, however, *indiscriminate* swabbing and the facile assumption that the person found to harbour KLB is responsible for a clincial case that we deprecate If circumstances point to a source of infection in the environment of a case, and particularly in closed communities where opportunities for transferring infection are relatively numerous, routine swabbing may be abundantly justified, but we are strongly of opinion that this procedure cannot be properly evaluated without simultaneous Schick-testing. Carriers revealed in this way need be segregated only until it is determined by further swabbing whether the condition is persistent and requires local treatment. Much more important than this in controlling an outbreak of diphtheria in these circumstances is to immunise the susceptible contacts.

ANDREW TOPPING,
President.

Fever Group, Society of Medical Officers of Health. NORMAN D. BEGG,
Hon. Secretary.

BLAST IN WATER

SIR,—The contribution by Goligher, King and Simmons, in your issue of July 31, has supplied a very useful and helpful guide to many of us who are seeing cases injured by under-water blast. This is a condition in which I have been interested for two or three years, and the following case is of significance in that it illustrates one of the difficulties in the diagnosis of the degree of intra-abdominal injury sustained.

A minesweeper was torpedoed at 04.00 hours and the order to abandon ship was given immediately afterwards. A rating clad in shorts and shirt, and wearing a life jacket, was swimming away from the sinking ship and when about twenty yards from the wreck one of the depth charges exploded. He said he felt as if he had stopped a football in the stomach, and he was winded for probably about half a minute after which he had a feeling of numbness in the abdomen but no pain. He swam about in the water strongly and moving his legs normally for four and a half hours until 08.30 when he was picked up by another minesweeper. He was rubbed down and given a cup of tea, which he enjoyed, but this he vomited ten minutes later. He had swallowed a good deal of fuel oil, and he continued vomiting for about one hour, but apart from the straining of the vomiting he had no abdominal pain. He was landed at 10.00 hours and walked to an ambulance, in which, about half an hour later and just before arrival at the hospital, he was seized with a sudden acute central abdominal pain which persisted until relieved by morphine. He was quite definite that morphine relieved the pain. Laparotomy was performed, and five perforations of the ileum were sutured. Recovery took place after a somewhat stormy convalescence with a pelvic abscess.

Now this rating was apparently fairly well and fit, with no marked symptoms, for six and a half hours after the injury. He could swim strongly, which he did for four and a half hours, and he could walk when ashore, without discomfort. Unfortunately there is no record as to the presence or absence of subserosal hæmorrhages. Were these perforations primary events, with a sudden onset of symptoms six and a half hours later, or were they secondary to interstitial hæmorrhages? The symptoms point strongly to the fact that perforations occurred in the ambulance, in which case they were secondary to hæmorrhages. If so, why did five perforations suddenly occur?

This case would seem to indicate the importance of careful observation of all who have been exposed to under-water blast, and extreme caution in passing over a man who is at the time showing no symptoms significant of severe intra-abdominal damage. It challenges the belief of Palma and Uldall quoted in your annotation (p. 133), that the intensity of the abdominal pain is a fair measure of the gravity of the injury.

At a Naval Hospital. P. G. C. MARTIN.

PURPURA OF THE SKIN

SIR,—In your issue of Aug. 28 Dr. Burnett has invited me, in effect, to write an article different in scope and purpose from the one you printed for me on Aug. 7. He thinks that the presence or absence of thrombocytopenia is a basic factor in all cases of purpura, but Macfarlane's review (*Quart. J. Med.* 1941, **10** N.S., 1) discourages this idea. Actually thrombocytopenia has nothing to do with purpura simplex—and indeed with most benign purpuras, which formed the bulk of my cases. Dr. Burnett suggests that my series should have been analysed into cases associated with platelet defect, or with normal platelets, giving their respective bleeding, clotting and clot retractility times. But as these

findings are known to be normal in many categories I enumerated, such a classification seemed unhelpful. (Haden and Schneider 1941, cited in my article, give just this type of information.) Thus I found no thrombocytopenia and no alteration in bleeding, clotting, and retractility times in even the severest cases of purpura simplex, Schönlein-Henoch, and cardiovascular purpura; whereas the findings in thrombocytopenic purpura, blood diseases, and hæmorrhagic diathesis simply confirmed standard work. I have no experience myself of "qualitative platelet defect" although I have read the papers of Glanzmann, Jürgens, &c.—and also the criticism of their work by Witts (*Guy's Hosp. Repts.* 1932, 82, 465) and Macfarlane. So I had to seek clinical association—still, I hope, a useful quest.

Dr. Burnett is right to stress that because purpura occurs (say) at the puerperium it is not necessarily due to the puerperium; drugs, scurvy, and so forth must be considered. That is exactly what I did. Menstruation, pregnancy, and the puerperium were associated with skin-purpura in a dozen cases where they are classified under other headings. In my series I found purpura of the skin more commonly associated with certain general factors such as sex, the rheumatic state, infection, and heredity than with blood abnormalities. When times are more spacious I should like to publish details of some of my categories.

St. Andrew's Hospital, E.3. ELI DAVIS.

PLANNING WITHOUT A PLAN

SIR,—The article by Dr. Robb-Smith in your issue of Aug. 28 is a great service to the planning of our health services. With almost all of it I disagree but with none of it do I quarrel, any more than the writer quarrelled with me in his criticism of what I have previously written. We are both striving for the same aim, so well put in the quotation he gave from Mumford, "to bring the geographical and economic facts in harmony with human purpose." Any figures I have ever put forward were intended, as I made clear in *Health for All*, to stimulate such studies as that of Dr. Robb-Smith. Disagreeing as I do with his conclusions, I recognise that his is the right approach to the subject. What a contrast with the method of the council of the British Medical Association. Their memorandum (*Brit. med. J.* Aug. 7) is clearly seen, in the light of this article, as "plans without planning."

I cannot in your letter page answer all the points to which I would like to refer. Let me say briefly that I disagree with the conception of a health unit of 250,000 and the whole paraphernalia of key hospitals, cottage hospitals and the like. The answer to Robb-Smith's pessimism—I will not call it defeatism—about the number of doctors is not in their concentration at a few large centres but their widest possible diffusion throughout the country; the 100,000 population health unit with its large general hospital, in an elastic structure, meets the needs of the people better than any other suggested.

Secondly, I am glad that Dr. Robb-Smith sets a standard of hospital staffing so much higher than I put forward. I have so often been called utopian and accused of impracticable schemes that it is a change to be accused of parsimony. My figures were an attempt to compromise between the most idealistic and the possible, a consideration for which we "planners" have more use than our opponents give us credit. I have discussed these figures with surgeons and physicians all over the country and almost all have agreed with them. I cannot elaborate the matter now, but I would make one slight correction which does affect the argument; my "seniors" were not to be taken as the equivalent of "registrars."

I do not, however, agree that a 47% increase in medical personnel is needed for a comprehensive national health service. Dr. Robb-Smith overlooks the many factors in a salaried service that would save time and labour. So far as senior surgeons and physicians are concerned the time saved from travelling between hospitals would, alone, be enormous. One consultant was boasting to me a few days ago that he was on at thirteen different hospitals and visited them all in addition to his private practice. Technical assistance of every kind would also be organised and extended. Some increase in staffs there must be, but redistribution, organisation, avoidance of overlap and wasted time would make the necessary increase well within the bounds of the same space of time as the fundamental organisation of the service will in any case require. No-one has suggested that it will happen overnight. But if Robb-Smith were correct, then the 47% increase in doctors he advocates reveals how bad our existing service must be in some places and should strengthen our determination to replace it by an entirely new and better service.

In so far as more doctors are required the solution lies in the plan adopted; but some lessons could be taken from that other planned medical service which has shown, to adopt Mr. Churchill's words, that no other form could have withstood such blows as Fascism has dealt it, the health service of the USSR. Dr. Robb-Smith mentions that a Russian doctor has a 5- or 6-hour working day; but in Russia the full plan was made and the shortage of doctors was got over by every doctor working two or even three such days until more students could be educated; medical education was made free to all who were suitable; and the number of doctors in Russia is now increasing at the rate of 25,000 per year (*Brit. med. J.* Aug. 28). A plan must include devices for the interim as well as ideals for the fully developed stage.

But it is surely no argument that because there are not enough of a certain kind of doctor we should hesitate to put into operation the greatest possible measure of the plan we have made. The Battle of Britain would not only have been lost but never even fought if Robb-Smith's conclusions were valid. It is vital that we make a start now with every necessary plan so that in five years' time Dr. Robb-Smith and others will be able to write another analysis showing how good the service is compared with today; and how, as will always be the case with a health service, it can be made better.

Richmond, Surrey. D. STARK MURRAY.

SIR,—I have read Dr. Robb-Smith's article with considerable interest, but take strong exception to a gratuitous insult in it, which reads: "The real problem arises if there is a doctor whom no-one or very few will choose. Perhaps he might become a hospital administrator or be put in charge of the regional health department!" If this is the sort of hospital administrator or doctor he would suggest be put in charge of a regional health centre, then all I can say is "God help the hospital or regional health centre." As Dr. Robb-Smith has made his suggestion for the disposal of the doctor who is not generally acceptable to patients, I fearlessly suggest that such a doctor be appointed a pathologist or pathological director.

ERNEST C. HADLEY,
Honorary Secretary of the Medical Superintendents' Society.

"AVIATION MEDICINE"

SIR,—May I correct certain erroneous impressions which your review of my book (April 24, p. 528) has created. Unlike the books of Bauer (1936) and Armstrong (1939) it was not written for the specialist and the comparison with them is unwarranted. While it is true, as you say, that my main subject is physical education, I have been a pilot for many a year, and did research on aviation medicine at a time when it was not acknowledged as a separate branch of medicine. At the Lourenco Marques congress of the South African Medical Association in 1938, I deprecated the lack of interest then taken in this field and demanded the immediate creation of an adequate organisation for research and teaching. Nothing however was done, and at the outbreak of the war no such service was available in this country. Then, at the request of various air schools, I was asked by the late Colonel R. F. A. Hoernle, OC Army Education, Union Defence Force, to take over the lectures on aviation medicine at various camps; for two and a half years I combined this with my duties as consultant in physical education.

After almost every lecture I had inquiries about suitable reading, without being able to give a satisfactory reply. Armstrong's fine book was not written for flying personnel. Their need was my sole reason for accepting the publisher's invitation to print my lecture notes in

book form. War conditions delayed its appearance and further knowledge has of course accumulated in the meantime; but I hold that it was and still is unnecessary to include in such a course of lectures all recent advances in aviation medicine. Even had this been possible, it would not have been permissible during the war.

I notice with satisfaction that you do not make any factual criticism of my book. Actually no single misstatement of importance has been brought to my notice by any reviewer, and I have heard from combatant officers and men in different theatres of war that the book has introduced them to a vital subject of which they had little or no knowledge. That my references "range from the *Psalms* to the *Saturday Evening Post*," instead of following the orthodox and more boring pattern which so many people admire but do not read, seems to have been widely appreciated.

Johannesburg. E. JOKL.

DIPHTHERIA IN THE INOCULATED

SIR,—The state of affairs to which Dr. Neubauer called attention in your issue of Aug. 14 (p. 192) is of importance also to anæsthetists and surgeons. If an inoculated child can present a diphtheritic throat indistinguishable from a simple tonsillitis there will be unrecognised cases among the child population, some of them suffering from toxic myocarditis. Such a child may be considered fit for tonsillectomy, when the tonsillar enlargement is simply due to œdema following the infection, or for some unrelated operation, when anæsthesia would be fraught with danger and chloroform likely to be disastrous. The condition of the heart muscle is so important in relation to induction of anæsthesia that a chapter on cardiology might well be incorporated in textbooks on anæsthetics; perhaps some simple exercise-tolerance test, to be carried out in bed or on a trolley, would give a danger signal. A blood-pressure reading by the anæsthetist might, Dr. Neubauer suggests, be of more value than the stethoscope.

Birmingham. J. W. RIDDOCH.

HOSPITAL POLICY

SIR,—A committee consisting of two representatives of the medical committees of each of the London undergraduate teaching hospitals has been formed with the object of coördinating the views of the medical staff of these hospitals. At a meeting on Aug. 17 the following resolution was passed.

This meeting regards it as essential that freedom of expression in medical matters and hospital policy, and freedom of medical practice, be preserved in hospitals in any postwar reconstruction; and that a medical committee should be the advisory body to the governors of an institution on medical matters.

GEOFFREY BOURNE, St. Bartholomew's Hospital. (Chairman.)
W. D. DOHERTY, Guy's Hospital. (Hon. Secretary.)

WE welcome, very cordially, a new contemporary in *Transatlantic* published at 1*s.* by Penguin Books Ltd. and edited by Geoffrey Crowther from 110, St. Martin's Lane, London, W.C.2. The object is to help the British to a better understanding of American affairs and American life, and paper has been allocated to it for this purpose; but it is an independent British journal, enjoying no subsidy and suffering no control, and it will not paint the United States in brighter colours than sober friendliness dictates. "If we are not to succumb to our enemies," says the first editorial, "we must keep close to our friends." And "in the great issues of Civilisation *versus* Barbarism, of Freedom for the human spirit *versus* Regimentation for the human soul, of Welfare *versus* Power, of Butter *versus* Guns—on all these great issues, so long as they keep their faith, America and Britain will always be on the same side." Meanwhile *Transatlantic* finds time to be entertaining as well as sane.

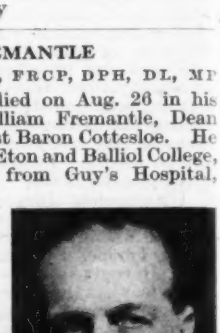
Hospitals' Day in the London area will be held this year on Tuesday, Oct. 5. Suggestions and offers of service should be sent to the London Hospitals Street Committee at 36, Kingsway London, W.C.2.

Obituary

FRANCIS E. FREMANTLE

KT, OBE, DM, CHM OXFD, FRCS, FRCP, DPH, DL, MP

Sir Francis Fremantle, who died on Aug. 26 in his 72nd year, was fourth son of William Fremantle, Dean of Ripon, and grandson of the first Baron Cottesloe. He was born in London, educated at Eton and Balliol College, Oxford, and qualified in 1897 from Guy's Hospital, where he edited the *Gazette*. After holding a series of house appointments at Guy's he went through the South African War as field surgeon, volunteered for plague duty in the Punjab, and was special correspondent of the *Lancet* during the Russo-Japanese War 1903–04. In 1902 he was appointed CMO for Herts, becoming chief school MO in 1908 and holding both posts until 1916, when he was retained as consultant. He lectured on public health and tropical hygiene at several London medical schools, and the Society of MOHs elected him their president. In 1902 he joined the Herts Yeomanry as surgeon-captain; he became sanitary officer East Anglian division and during the war of 1914–18 was DADMS (San.) in Egypt and Mesopotamia with the rank of lieut.-colonel RAMC (T). From 1906 he was prospective Unionist candidate for Rotherhithe, but on the eve of election in 1910 he was disqualified by a ruling, since removed, against MOHs and he first entered Parliament in 1919 as member for St. Albans, occupying the seat until his death. For 18 years he was chairman of the Unionist Health and Housing Committee and his other parliamentary activities were set out in our last issue by Medicus MP.



Elliott & Fry

This curriculum vitæ is the more remarkable because it was instinct with the desire for social service. From his youth he knew he would inherit a considerable estate (at Bedwell Park), and in his Oxford days he determined to enter politics; if he took good medical degrees he would be the better able to interpret medical problems to his political companions. He had no particular flair for examinations; passing them was for him hard work. And the assiduity with which he read the *Times* during his period at Guy's was the subject of some jest among his fellow students, with whom he was nevertheless popular. There was no jesting, however, about the trenchant letters from South Africa which appeared in the *Gazette*, for his exposure of the shortcomings of the Army medical services was a contributing cause to the inquiry which followed that war; he was indeed asst. secretary to the departmental committee charged with reorganising these services. His tenure of the county health appointment was indefinitely prolonged by the opportunities it offered him of planning the background of people's lives.

In his parliamentary life he accepted the doctor's mandate (to quote the words of a Chadwick public lecture he gave in 1937) to express the special experience of his profession and the knowledge of life in every phase of it and in every section of the community—both on matters of health and on those of general policy and administration. He regarded himself as in the long line of succession beginning with Dr. John Somerset, physician to Henry VI, who was Chancellor of the Exchequer 1440–46. On the medical MP falls especially the privilege of dealing fearlessly with the awkward topics—sexual questions and marriage, betting, licensing, Sunday trading, and moral and ecclesiastical problems. As chairman for 18 years of what is now called the Conservative Social Services Committee something of the execution of this privilege may be given in his own words. "On Feb. 20, 1924, the committee met for the first time. In March I prepared a memo for them on building by collective enterprise, especially public utility societies. In May, Neville Chamberlain asked me for a

memo on provision of hospitals. Lord Eustace Percy and Sir Ian Roberts prepared memos on a new housing policy, and we were largely occupied with amendments to Mr. Wheatley's housing and building materials bills. In 1925 we were concerned with LCC slum clearance, rent restriction, and contributory pensions, which Chamberlain and his henchman, Kingsley Wood, came twice or more to discuss with us. In each succeeding year we have met monthly, or oftener as required, mainly to deal with current legislation, and have had leading authorities from outside, as well as the Ministers concerned directly and indirectly, to talk to us and be heckled. We prepared amendments, put up speakers in debate in the Chamber, and encouraged local and individual views. Now the committee has started serious work on the Beveridge report. I think it has done good work, chiefly in interesting MPs. It is, however, surprising that the women MPs have hardly ever attended." Nurses and midwives do not come in this list, but Fremantle had much to do with improving their status and working conditions. For the Institute of District Nurses, writes its vice-chairman, he was always ready to give his help. "I wish," he adds, "there were more people like him."

Sir Francis Fremantle married in 1905 Dorothy, only daughter of Henry J. Chinnery, JP, of Fringford Manor, Bicester. They had one son.

FREDERICK JOHN CLEMINSON

M CHIR CAMB, F R C S

Mr. F. J. Cleminson, consulting aural surgeon to the Middlesex Hospital, died of pneumonia at his home at Willingale, Ongar, on Aug. 21. He was the first director of the Institute of Otology at the Middlesex, opened in 1927 through the generosity of his uncle, the late Thomas Ferens. In 1938 Cleminson retired from his extensive practice and from his appointments on the staff of the Middlesex, the Evelina Hospital, and the Heart Hospital to give all his energies to his work at the Ferens Institute, and it was a bitter disappointment to him when in the following year the institute had to be closed on the outbreak of war. But his Essex home gave him opportunities for his chosen hobbies of ornithology and sailing. The equipment and the library of the institute, though not the building, have survived the blitz, its funds have been accumulating, and when it reopens after the war it will be a worthy memorial to its first director.

Frederick John Cleminson was born in 1878, the son of the Rev. J. R. Cleminson of Hull, and educated at Kingswood School, Bath, and Caius College, Cambridge. He received his medical training at University College Hospital, graduating BChir in 1909 and taking the fellowship three years later.

"At Cambridge," writes O. M. who went up with him in 1897, "Clem soon showed his aptitude for medico-scientific subjects, and he got his double first in the natural sciences tripos without any undue exertion. Indeed, had single-minded application to work been necessary he might have missed it, for he wisely refused to become the complete scholar, but gave full scope to his real genius for friendship. His range was both wide and deep; he drew out the best from a variety of men—rich and poor, scholarly and sporting, studious and idle. After taking our degrees in 1901, we joined up as a coaching partnership in anatomy and physiology. We also took reading parties in the Easter vacations when we really worked hard, with extraordinarily pleasant intermissions for play. When he tore himself away from the congenial atmosphere of Cambridge to qualify and work in London, he made new friends without losing his earlier ones. As an example, in 1928 he arranged a little dinner for some of us who had worked together for Part II of the tripos in 1901—T. R. Elliott, R. Foster Moore, W. M. Mollison. We invited some of our lecturers—Gowland Hopkins, Walter Fletcher, C. S. Myers, and H. K. Anderson, and a very successful evening it was."

Cleminson was deeply interested in the prevention of deafness, and his skill in the management of children, recognised during his clinical assistantship at the ear, nose and throat department of the Great Ormond Street, was confirmed by his appointment to the Evelina. He made a special study of sinusitis in children which was the subject of one of his rare but illuminating contributions to the section of otology RSM of which he was one time president. At the section of laryngology he discussed headache associated with nasal disease and the applications of radium and radon in which he was much interested. He was more at his ease at the international club he helped to found at Groningen. But he was always concerned with doing rather than with speaking or writing. No surgeon ever gave more wholehearted service to his patients, and none was more beloved by them.

In 1906 he married Miss Sarah Smucker of Philadelphia, and he leaves her with one son and two daughters.

ATHELSTANE ILIFF SIMEY

M D CAMB, F R C P

Simey's death will be felt as a personal loss by his innumerable friends. For 23 years he was medical officer to Rugby School, where his outstanding achievements were the introduction of a substantial evening meal and the abolition of useless quarantine. He was born at Sunderland in 1873, youngest of the three sons of Ralph Simey, DCL, all of whom were educated at Rugby. Here he became head of the school. He went to King's College, Cambridge, with a classical scholarship, and took a first-class in the classics tripos before starting medicine. In 1901 he qualified from the London Hospital, where he stayed to be medical registrar, and he was also outpatient physician at Victoria Park before returning to Rugby in 1908. Farquharson and Dukes, his predecessors, had already established their fame as school doctors. Simey, soon after his appointment, advocated the substitution of a substantial evening meal for the customary bread-and-jam tea supplemented by private purchases. Wasteful, he said, and the growing boys who needed a good supper in the evening were not only those whose parents could afford to send hampers from home. Victory was not easy, and only after a few converts had tried the experiment and found that cooks did not leave, or could be replaced, did the other housemasters follow suit. Thus Rugby was the first school to provide suppers with a substantial dish in them. Every school has followed its example.

Dean, Rugby

It was Simey's sense of justice which first made him consider whether it was fair to quarantine boys exposed to infections in the holidays, while freely sending boys home at the end of term after exposure at school. He preferred epidemics of measles "little and often" rather than in bulk. His policy succeeded, and he was the real author of the regulations in the MOSA code which allowed the return to school of boys who had been exposed to infection if they were kept away from its source as soon as recognised. Many persisted with the safety-first method, but epidemic history has supported Simey. As a physician, on the other hand, he was if anything too careful, and he thoroughly enjoyed the *Punch* cartoon with Tom Brown being told by his father to be tough and by his mother to report the slightest cold to Dr. Simey. Certainly the boys thought he took too many precautions, but Simey never bred neurotics. He served the Hospital of St. Cross with as much zeal as he served his school. He was its physician and radiologist, sometime chairman and secretary to the medical board, and spared no pains to nurture its rapid growth. The nursing staff there, as well as in the school sanatorium, recognised him for what he was.

When after 23 years devoted service to the school he felt the time had come to make way for a younger man Simey migrated to Exeter as physician to the Exmouth Hospital, but finding consulting practice too great a strain he built a house on the edge of the New Forest where his garden and the birds were a perennial delight to him. His last three years were spent at his cottage at Dockray, under Helvellyn. Though he had left Rugby twelve years ago, not a Christmas passed but he wrote to all his friends there.

Nothing was too much trouble for him. He was an idealist, and his life was marred by disappointments. Perhaps he might have seen the new sanatorium built if he had been content with less and smaller rooms. His advocacy of pasteurisation fell upon dull ears. But he knew no malice and made no enemies. His devoted wife, who shared all his interests, will have the satisfaction of assurance that Simey's unobtrusive pioneer work in nutrition and epidemology has been copied and not found wanting.

Notes and News

CONTROL OF NURSES

EFFECT OF THE AMENDING ORDER

THE Employment of Women Order which came into force two years ago excluded nurses from the regulations controlling other women between 18 and 40. The Minister of Labour and National Service has now amended the principal order to include nurses in these age-groups except those who are members of the Civil Nursing Reserve. Under the new amendment (no. 1278, dated 31.viii.43) all nurses and midwives, after Sept. 20, must obtain their employment through the appointments office of the Ministry in the area in which they live. The aim is to prevent the overstaffing of hospitals (such as the large teaching hospitals) which can easily engage as many nurses as they require, and to encourage women applying for service in them to enter other neighbouring hospitals which are short of staff. They have always had this option, of course, but when refused by the hospital of their choice they are apt to give up nursing and turn to other occupation. Qualified nurses are now to be required to follow their own profession rather than take up other work, so that a nurse refused by one hospital will now either have to enter another in the area, or remain out of work (and out of pocket) until the Ministry sees its way to direct her into other employment. It is hoped that this narrowing of her choice of job will help to staff mental and fever hospitals, sanatoriums, and other institutions now lacking nurses.

The amendment offers various exemptions. Thus, though employers are required to engage nurses and midwives through an appointments office, hospitals and similar institutions will be freely granted certificates exempting them from this obligation in respect of nurses of the grade of ward sister and above (though the Ministry must ratify any appointments made); and also in respect of vacancies for student nurses and pupil midwives. Students will thus be able to go on choosing where they will train, as long as there are vacancies for them. In a hospital granted these exemptions the only grade affected by the new order would be that of staff nurse; and it is difficult to see any great advantage from the plan. Many teaching hospitals employ students in their final year of training as staff nurses, and these would presumably come under the exemption covering students. In sanatoriums and mental hospitals it is unfortunately rare to find state-registered nurses holding the appointment of staff nurse, or even of charge nurse (the equivalent of a ward sister in a general hospital). In any case qualified staff nurses form a relatively small proportion of the staff of a teaching hospital, and the gain to neighbouring hospitals from control of their employment seems likely to be slight.

Nurses engaged in private practice will be given permits to continue in their work provided they can produce evidence that they are employed for 10½ months in the year; no permits will normally be granted to women under 30. The amendment does not affect qualified nurses who have already given up their profession and taken other employment in factories and elsewhere; but these are being interviewed, and when they seem suitable attempts are being made to persuade them to return to nursing.

The Minister has also decided to put into operation the order requiring newly qualified midwives to practise their profession for a year. As a temporary measure, and because the shortage of midwives is acute, no practising or recently qualified midwife will be allowed to take employment other than midwifery for the next six months (until February, 1944); after that the position will be reviewed.

The disquieting aspect of the amending order is that it makes no attempt to integrate the nursing service or to plan it regionally. As it stands it may even have an adverse effect on recruitment. The general teaching hospitals can only take a limited number of students, and at present girls contemplating nursing, and finding themselves excluded from the hospital and type of training of their choice, are turning to other occupations. If they find that the choice of work open to the qualified nurse is also being restricted, they will have still less incentive to begin. A regional plan under which a nurse passed in rotation through the general and special hospitals of her area, as part of her routine course for the SRN, would not only help to solve the staffing and recruiting problems of the hospitals, but would give the nurse a wider practical training and would, we have little doubt, attract the qualified woman into those branches of nursing which she avoids at present largely through ignorance of their scope.

Naval Honour

The RNVR officer's decoration has been awarded to Surgeon Lieut.-Commander J. O. Clyde, MRCS.

Medical Casualties

The following casualties among RAMC officers have been announced:

Wounded.—Captain J. S. Montgomerie, MB ST. AND.

Prisoners of War.—Captain Arthur Barber, MD LOND.; Lieut.-Colonel H. C. Benson, MB EDIN.; Captain David Christison, MB GLASG.; Major W. H. Dowell, MRCS; Captain A. W. Frankland, BM OXFD.; Major P. B. Hanbury, MRCS; Major N. C. Lendon, B CHIR CAMB.; Captain J. S. McConnachie, MB ABERD.; Captain K. C. Matheson, MB GLASG.; Captain T. S. Protheroe, MRCS; Captain Louis Sefton, MRCS; and Captain R. G. B. Young, MB EDIN.

DR. CHRISTABEL SYBIL NICHOLSON (née Eyre) has been released from Holloway prison where she has been detained under defence regulation 18B since May, 1940. At her trial held in camera the following year she was acquitted and taken back to detention.

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Births, Marriages and Deaths

BIRTHS

CHATAWAY.—On Aug. 26, at Mombasa, E. Africa, the wife of Dr. J. H. H. Chataway, Colonial Medical Service—a son.

LE VAY.—On Aug. 28, at Oxford, to Dr. Marjorie Le Vay (née Cole), wife of Lieutenant A. D. Le Vay, RAMC—a son.

MITCHELL.—On Aug. 29, at Radlett, the wife of Dr. T. Carlyle Mitchell—a son.

SMITH.—On Aug. 25, the wife of Dr. Donald Bell Smith—a son.

SWANN.—On Sept. 1, in London, the wife of Surgeon Lieutenant G. F. Swann, RNVR—a son.

THOMPSON.—On Aug. 29, at Exeter, the wife of Major Denis Thompson, RAMC—a son.

MARRIAGES

CORCOS—BROOKSBANK.—On Aug. 17, at Nottingham, Michael Geoffrey Corcos, lieutenant RAMC, to Bettina Mary Brooksbank, SRN.

MCKENDRICK—GABRIEL.—On Aug. 27, at Ruislip, George Donald William McKendrick, BM, to Evelyn Gabriel.

WILLIAMS—KEENE.—On Aug. 21, at Karachi, Thomas Meurig Williams, lieut.-colonel IMS, to Chris Keene.

DEATHS

FRAZER.—On Aug. 31, Edward FitzGerald Frazer, FRCSI, of Brighton.

HUNT.—On Aug. 28, at Gloucester, John William Hunt, MB LOND., late of Colonial Medical Service.

JELLY.—On Aug. 28, at Lytham, George Aubrey Jelly, FRCSE, DPM, aged 71.

LEES.—On Sept. 3, at Worthing, Charles Archibald Lees, CBE, MRCS, aged 73.

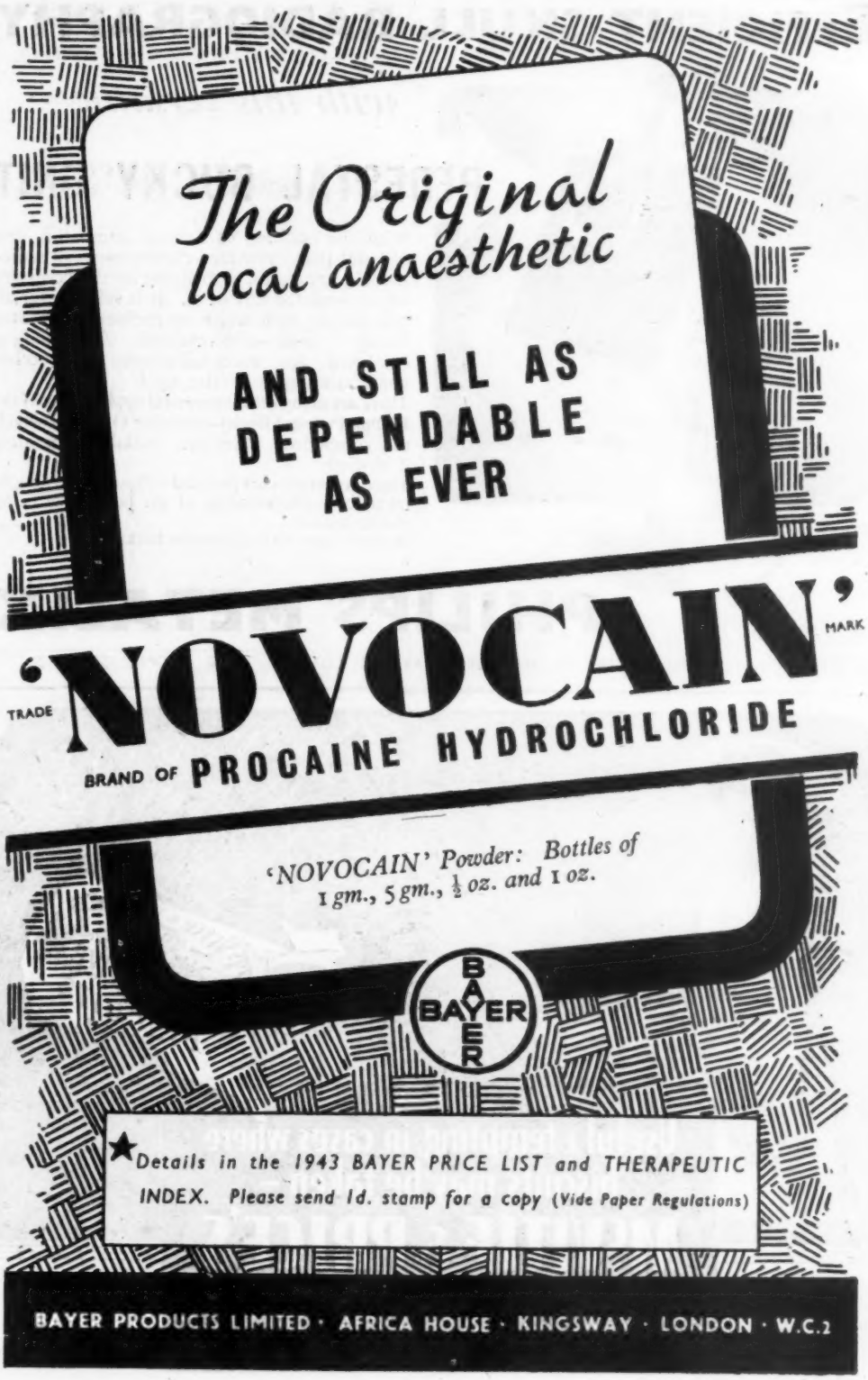
O'NEILL.—On Aug. 24, Gregory John Lamb O'Neill, MB EDIN., of Sydney, NSW.

PASTEUR.—On Sept. 1, at Warwick Park, Tunbridge Wells, William Pasteur, CB, CMG, MD LOND., FRCP, aged 87.

PAULLEY.—On Sept. 1, at Cheltenham, Job Nathaniel Legge Paulley, MRCS, JP, formerly of Pulham Market, Norfolk, aged 87.

SCOTT.—On Sept. 1, at Midhurst, Sussex, John Easton Scott, MB EDIN., aged 65.

The fact that goods made of raw materials in short supply owing to war conditions are advertised in this paper should not be taken as an indication that they are necessarily available for export.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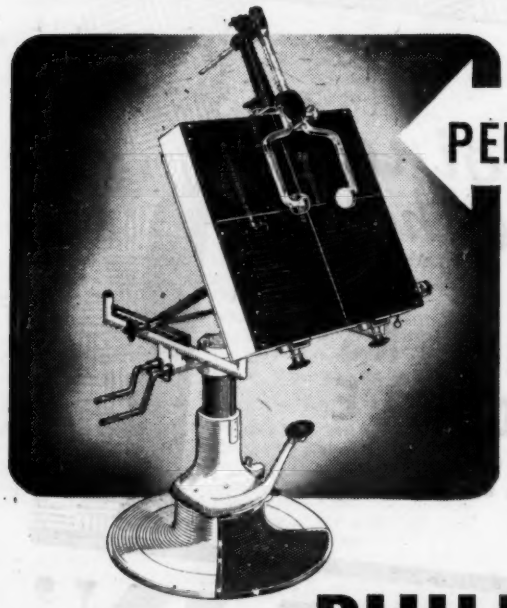

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For this reason the practitioner generally prefers to prescribe certain stimulating foods such as meat extracts, soups, and home-made broths.

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Fifty-seven cases of menstrual delay were treated by injection of 1 mg. (2 ampoules) 'Prostigmin' on 3 consecutive days after endocrine disorders had been ruled out. If menstrual flow was not established within 72 hours a tentative diagnosis of pregnancy was made until confirmed by the Friedman test or clinical observation. A normal menstrual flow was produced in all those who were not pregnant, and those whom pregnancy was subsequently confirmed successfully continued their pregnancies.

The number of injections required to induce menstruation varied, some needing 3, some 2 and others only 1; occasionally 4 were required. (Jour. Amer. Med. Assoc., May 8, 1943, *122*, 81.)

Removal of X-ray Intoxication Symptoms

The intramuscular injection of an ampoule of 'Benerva' Forte (25 mg.) daily proved very beneficial in combating vomiting and other forms of X-ray intoxication.

Of 35 patients with marked X-ray intoxication symptoms 15 responded very well, so that a complete remission was obtained. In 12 cases, 7 of them severe cases, an appreciable improvement was found. In 8 cases no effect could be found, 3 of these being regarded as failures. Sometimes one to two injections were sufficient to abolish completely the symptoms. (Radiologia Clinica, 1942, *11*, p. 349.)

Treatment of Epistaxis with Vitamin C

'Redoxon' (vitamin C) has proved of value in 16 cases for the treatment of severe nose-bleeding, which could not be stopped by any of the other methods tried. One gram (2 ampoules of 'Redoxon' Forte) was injected intravenously, and if the bleeding did not stop within a few minutes the injection was repeated either with the same dose or, if it was abating, with 0·5 gm. (La Semana Medica, 1942, p. 312.)

Encouraging Results of Vitamin E Therapy

Successful results were obtained with the use of vitamin E therapy in 5 patients, 3 of whom were suffering from peripheral neuritis, with the Guillain-Barre syndrome, 1 from amyotonia congenita, and 1 from either amytrophic lateral sclerosis or muscular dystrophy of the Aran-Duchenne type.

The dosage used was 10 mg. of 'Ephynal' 3 times a day for varying periods, being increased in one case to 75 mg. a day. In all a striking increase in muscular strength and tone occurred.

According to the author, "further clinical trial of synthetic vitamin E in neuromuscular affections is warranted." (J. Nerv. & Ment. Dis., 1942, *96*, p. 184.)

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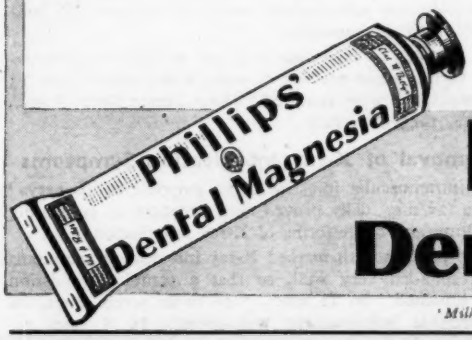

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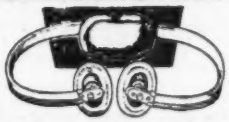

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Applications must be sent not later than 20th September to the Secretary of the Royal College of Surgeons, Lincoln's Inn-fields, W.C.2, from whom forms of nomination and further particulars may be obtained.

KENNEDY CASSELS, Secretary,
Mackenzie Mackinnon Research Fund Committee.
11th September, 1943.

Royal College of Surgeons of England.

ELECTION TO THE COURT OF EXAMINERS.

Notice is hereby given that the Council on the 11th November, 1943, will elect six members of the Court of Examiners. Of the Examiners retiring in rotation, two (Mr. R. Davies-Colley and Mr. G. T. Mullally) do not seek re-election, while the other four (Mr. V. Zachary Cope, Mr. C. E. Shattock, Mr. E. W. Riches, and Mr. W. H. C. Romanis) are eligible and seek re-election.

Fellows of the College desirous of becoming candidates for the office must make application in writing to the Secretary on or before Monday, 4th October.

11th September, 1943. KENNEDY CASSELS, Secretary.

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(UNIVERSITY OF LONDON)

WAR SURGERY OF THE NERVOUS SYSTEM
20-24th September

Monday, 20th Sept.	10 A.M.	The Anatomy (Surgical) of the Skull and Brain.	Mr. G. C. Knight, M.B., F.R.C.S., M.R.C.S., L.R.C.P.
	10.30 A.M.	Mechanism and Nature of the Injuries of the Skull.	Mr. G. C. Knight, M.B., F.R.C.S., M.R.C.S., L.R.C.P.
	11.30 A.M.	Mechanism and Nature of the Concomitant Injury to the Brain.	Mr. G. C. Knight, M.B., F.R.C.S., M.R.C.S., L.R.C.P.
	2 P.M.	Pathology of Wounds of the Nervous System: (*a*) Injuries to the Brain. (*b*) Wounds to the Spinal Cord and Peripheral Nerve Injuries.	
Tuesday, 21st Sept.	10 A.M.	Head Injuries in Desert Warfare.	Mr. D. W. C. Northfield, M.B., B.S., F.R.C.S., L.R.C.P., L.D.S. R.C.S.
	11.30 A.M.	Head Injuries in Desert Warfare (*contd.*).	Mr. D. W. C. Northfield, M.B., B.S., F.R.C.S., L.R.C.P., L.D.S. R.C.S.
	1.30 P.M.	War Injuries of the Spinal Cord.	Surg. Captain Lambert Rogers, F.R.C.S., F.A.C.S., F.R.A.C.S.
	2.30 P.M.	Demonstration on the Cadaver of Operations on the Spine.	Surg. Captain Lambert Rogers, F.R.C.S., F.A.C.S., F.R.A.C.S.
Wednesday, 22nd Sept.	10 A.M.	Surgical Sequelæ of Wounds of Skull and Brain.	Mr. G. C. Knight, M.B., F.R.C.S., M.R.C.S., L.R.C.P.
	12.15 P.M.	Use of X-rays in the Diagnosis of Head Injuries.	Major J. Duncan White, M.B., Ch.B., D.M.R.E.
	2 P.M.	Disorders following Head Injuries.	Dr. J. Purdon Martin, M.D., F.R.C.P.
	3.15 P.M.	Medical Aspects of Head Injuries.	
Thursday 23rd Sept.	10 A.M.	Some Sequelæ of War Wounds of Skull and Brain.	Mr. Harvey Jackson, F.R.C.S., M.R.C.S., L.R.C.P.
	11.30 A.M.	X-rays in War Injuries of the Spine.	Major J. Duncan White, M.B., Ch.B., D.M.R.E.
	2 P.M.	Medical Diagnosis of Spinal Injuries.	
	3.30 P.M.	Mental Sequelæ of War Injuries.	
Friday, 24th Sept.	10 A.M.	The Processes of Regeneration after Nerve Injury.	Mr. J. Z. Young.
	11.30 A.M.	Peripheral Nerve Injuries: (1) Diagnosis.	Prof. Seddon, F.R.C.S., M.R.C.S., L.R.C.P.
	2.15 P.M.	Peripheral Nerve Injuries: (2) Treatment.	Prof. Seddon, F.R.C.S., M.R.C.S., L.R.C.P.
	3.15 P.M.	Care of the Bladder in Injuries of the Nervous System.	Mr. Clifford Morson, C.B.E., F.R.C.S.

The fee for the Course will be one guinea, but in certain cases the fees for serving officers recommended by their Director-Generals are paid by their Military Authorities. Applications for admission should be sent to the DEAN, British Postgraduate Medical School, Ducane-road, W.12.

Further War Courses will commence as follows:—

WAR MEDICINE COURSE	4TH-8TH OCTOBER, 1943
WAR SURGERY OF THE EXTREMITIES ..	18TH-22ND OCTOBER, 1943
THE SURGICAL CARE OF THE SOLDIER IN TRAINING	1ST-5TH NOVEMBER, 1943.

L. M. S. S. A.

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This Registered Hospital is situated in 130 acres of park and pleasure grounds. Voluntary patients, who are suffering from incipient mental disorders or who wish to prevent recurrent attacks of mental trouble; temporary patients, and certified patients of both sexes are received for treatment. Careful clinical, bio-chemical, bacteriological, and pathological examinations. Private rooms with special nurses, male or female, in the Hospital or in one of the numerous villas in the grounds of the various branches can be provided.

WANTAGE HOUSE

This is a Reception Hospital in detached grounds with a separate entrance, to which patients can be admitted. It is equipped with all the apparatus for the complete investigation and treatment of Mental and Nervous Disorders by the most modern methods; insulin treatment is available for suitable cases. It contains special departments for hydrotherapy by various methods, including Turkish and Russian baths, the prolonged immersion bath, Vichy Douche, Scotch Douche, Electrical baths, Plombieres treatment, etc. There is an Operating Theatre, a Dental Surgery, an X-Ray Room, an Ultra-violet Apparatus, and a Department for Diathermy and High-frequency treatment. It also contains Laboratories for bio-chemical, bacteriological, and pathological research. Psychotherapeutic treatment is employed when indicated.

MOULTON PARK

Two miles from the Main Hospital there are several branch establishments and villas situated in a park and farm of 650 acres. Milk, meat, fruit, and vegetables are supplied to the Hospital from the farm, gardens, and orchards of Moulton Park. Occupational therapy is a feature of this branch, and patients are given every facility for occupying themselves in farming, gardening, and fruit growing.

BRYN-Y-NEUADD HALL

The seaside house of St. Andrew's Hospital is beautifully situated in a Park of 330 acres, at Llanfairfechan, amidst the finest scenery in North Wales. On the North-West side of the Estate a mile of sea coast forms the boundary. Patients may visit this branch for a short seaside change or for longer periods. The Hospital has its own private bathing house on the seashore. There is trout-fishing in the park.

At all the branches of the Hospital there are cricket grounds, football and hockey grounds, lawn tennis courts (grass and hard courts), croquet grounds, golf courses, and bowling greens. Ladies and gentlemen have their own gardens, and facilities are provided for handicrafts, such as carpentry, etc.

For terms and further particulars apply to the Medical Superintendent (TELEPHONE: No. 2356 and 2357 Northampton), who can be seen in London by appointment.

RUTHIN CASTLE, NORTH WALES

A Private Clinic, the first in Great Britain, for investigation and treatment of all forms of disease, except infectious and mental

There is a steel and concrete Air Raid Shelter with heating and a lift to all floors

Inclusive charges — Apply SECRETARY — Telephone: Ruthin 66

PECKHAM HOUSE, 112, Peckham Road, London, S.E.15

Telegrams: "Alleviated, London" **Telephone: Rodney 2641-2642**

A Private Mental Hospital, for Ladies and Gentlemen suffering from Nervous and Mental Illness, where the amenities of a comfortable home are combined with full investigation and every well-established modern treatment.

Terms from 3¼ guineas weekly.

Illustrated Prospectus may be obtained from the Physician Superintendent.

CAMBERWELL HOUSE, 33, Peckham Road, London, S.E.5

Telegrams: "PSYCHOLIA, LONDON" — FOR THE TREATMENT OF MENTAL DISORDERS — *Telephone:* RODNEY 4242 (2 lines)

Completely detached Villas for mild cases. Voluntary Patients received. Twenty acres of grounds; own garden produce. Hard and grass tennis courts, putting greens, Recreation Hall with Badminton Court, and all indoor amusements. Occupational therapy, Calisthenics, Actino-therapy, prolonged immersion baths, shock and also modified insulin treatment. Chapel.

Senior Physician, Dr. HUBERT JAMES NORMAN, assisted by a resident Medical Staff and visiting Consultants

An Illustrated Prospectus giving fees, which are strictly moderate, may be obtained upon application to the Secretary

The Convalescent Branch is HOVE VILLA, BRIGHTON and is 200 ft. above sea-level

COURT HALL, KENTON, near EXETER

FOR THE TREATMENT OF EIGHT LADIES, VOLUNTARY, TEMPORARY AND CERTIFIED PATIENTS

CLIFFDEN, TEIGNMOUTH

FOR EARLY AND CONVALESCENT CASES — Recreational Therapies are held daily by skilled Leaders

The house stands high with spacious balconies and extensive views of the South Devon Coast. Beautiful garden. Own Dairy in 25 acres. Private road to beach

There is also a charming house, **EBWORTHY, MANATON, DARTMOOR**, situated in 20 acres, 1100 ft. up for bracing moorland air

Resident Physicians—BERTHA M. MULES, M.D., B.S. ANNE S. MULES, M.R.C.S., L.R.C.P. — *Telephones*—STARCROSS 259 and TEIGNMOUTH 249

SHAFTESBURY HOUSE

FORMBY-BY-THE-SEA
Nr. LIVERPOOL

Specially built and licensed for the care and treatment of a limited number of Ladies and Gentlemen suffering from NERVOUS and MENTAL breakdown. Voluntary and certified patients received. Ladies also admitted as Temporary Patients without certification. Terms moderate. *Apply*, RESIDENT PHYSICIAN, who may be seen in Liverpool, by appointment. *Tel. No.* 8 *Formby.*

CHEADLE ROYAL

CHEADLE
CHESHIRE

A Registered Hospital for MENTAL DISEASES, and its Seaside Branch, GLAN-Y-DON, Colwyn Bay, N. Wales

THE object of this Hospital is to provide the most efficient means for the treatment and care of PATIENTS of BOTH SEXES suffering from MENTAL and NERVOUS DISEASES. The Hospital is governed by a Committee appointed by the Trustees of the Manchester Royal Infirmary. VOLUNTARY, TEMPORARY, AND CERTIFIED PATIENTS RECEIVED

For Terms and further information apply to the MEDICAL SUPERINTENDENT *Telephone*: GATLEY 2231

THE OLD MANOR, SALISBURY

Telephone: 3216 & 3217

A Private Hospital for the Care and Treatment of those of both sexes suffering from MENTAL DISORDERS

Extensive grounds. Detached Villas. Chapel. Garden Produce from own gardens. Terms very moderate.

CONVALESCENT HOME AT BOURNEMOUTH

standing in 12 acres of ornamental grounds, with separate villas, tennis courts, etc. Patients or Boarders may visit the Home by arrangement.

Illustrated Brochure on application to the Medical Superintendent, The Old Manor, Salisbury.

HAYDOCK LODGE,

NEWTON-LE-WILLOWS, LANCASHIRE.

For the reception and treatment of PRIVATE PATIENTS of both sexes of the UPPER AND MIDDLE CLASSES suffering from Mental and Nervous Disorders, Alcoholism and Drug Addiction, either voluntarily, temporarily, or under certificate. Patients are classified in separate buildings according to their mental condition. Situated in park and grounds of 400 acres. Self-supported by its own farm and gardens in which patients are encouraged to occupy themselves. Every facility for indoor and outdoor recreation. For terms, prospectus, etc., apply MEDICAL SUPERINTENDENT. *Telephone:* Ashton-in-Makerfield 7311. *Telegraphic Address:* Wootton, Ashton-in-Makerfield.

CALDECOTE HALL

NUNEATON

WARWICKSHIRE

('Phone : Nuneaton 241)

Residential treatment of

"Nervous Disorders" & Alcoholism

(Certifiable cases are not received)

This beautiful mansion situated in the heart of the country (less than two hours from London by L.M.S.R.) and surrounded by charming pleasure grounds in which games and outdoor occupational therapy are available is devoted to the treatment of Alcoholism and "Nerves" by psychotherapeutic and ancillary methods.

Illustrated Brochure and particulars obtainable from A. E. CARVER, M.D., D.P.M., Resident Medical Superintendent.

THE MAGHULL HOMES FOR EPILEPTICS (Inc.)

MAGHULL, Near LIVERPOOL

Open Air Occupation and Recreation for Patients, Farming, Gardening, Football, Cricket, Tennis, Bowls, etc. School recognised by Board of Education.

FEES—

1st Class (men only)	.. .. .. from	£3 per week
2nd Class (men and women)	.. .. ..	37/6 ,,
3rd Class (men and women) supported by		
Public Assistance Committees	.. ..	27/6 ,,
Education Committees	.. ..	33/6 ,,
Private	.. ..	21/- ,,

For further particulars apply to—

C. EDGAR GRISEWOOD, A.C.A., 20, Exchange Street East, LIVERPOOL, 2

FENSTANTON

at "FIVE DIAMONDS," Chalfont St. Giles, Bucks

A Private Home for the Care and Treatment of a limited number of LADIES with Mental and Nervous Disorders. Certified, Voluntary, and Temporary Patients received. Mansion with 12 acres of ground (See *Medical Directory*, p. 2441.) Apply Resident Physician. Telephone: Little Chalfont 2046. Station: Chalfont and Latimer.

HEIGHAM HALL, NORWICH

PRIVATE MENTAL HOME for Nervous and Mental illness. All forms of treatment available. Fees from 4 gns. per week upwards according to requirements. Vacancies occasionally exist at reduced fees on the recommendation of the patient's own physician.

Apply to Dr. J. A. SMALL. Telephone : Norwich 20080

UNIVERSITY EXAMINATION POSTAL INSTITUTION

17, RED LION SQUARE, LONDON, W.C.1

Over 50 years' experience

POSTAL COACHING FOR ALL MEDICAL EXAMINATIONS

MEDICAL PROSPECTUS (36 pages)

sent gratis, along with List of Tutors, &c., on application to the Principal, 17, Red Lion Square, London, W.C.1. (Telephone: HOLborn 6318.)

Examining Surgeons:

FACTORIES ACT, 1937.

The following appointment as Examining Surgeon under the Factories Act, 1937, is vacant.

Applications should be sent to the CHIEF INSPECTOR OF FACTORIES, 78, Broadway, London, S.W.1.

District	*County*	*Latest date for receipt of application*
KIDSGROVE ..	STAFFORD ..	20TH SEPTEMBER, 1943

London Chest Hospital,

Victoria Park, E.2.

HOUSE SURGEON (B2) (Male or Female) required on 1st November with previous surgical experience, preferably thoracic. Salary £150 per annum, with full residential emoluments. R and W practitioners who now hold A posts may apply, when appointment will be limited to six months.

Applications, with copies of three recent testimonials, should be sent by 25th September to the SECRETARY.

London Chest Hospital,

Victoria Park, E.2.

HOUSE PHYSICIAN (B2) (Male or Female) required on 1st November. Applications from R and W practitioners who have been qualified more than three months cannot be considered unless they have been rejected by the R.A.M.C. Six months' appointment. Salary at the rate of £150 per annum, board, residence, and laundry provided.

Applications, with copies of three recent testimonials, should be sent by the 25th September to the SECRETARY.

London County Council.

Locum tenens ASSISTANT MEDICAL OFFICER required for indefinite period at LAMBETH HOSPITAL, Brook-drive, Kennington-road, S.E.11. Experience in radiotherapy desirable. Remuneration seven guineas a week, and full residential emoluments.

Application form obtainable (stamped addressed foolscap envelope necessary) from MEDICAL OFFICER OF HEALTH (S.D.2), County Hall, S.E.1, returnable by 20th September, 1943. Canvassing disqualifies.

The Belgrave Hospital for Children,

1, Clapham-road, S.W.9.

The Committee of Management invite applications from registered medical practitioners, Male and Female, for the appointment of RESIDENT HOUSE OFFICER (A), vacant 1st October. Salary is at the rate of £100 per annum, with full residential emoluments. The successful candidate would become eligible for a further emolument in the first-aid post if willing and able to undertake duties. Practitioners within three months of qualification and liable under the National Service Acts may apply, when appointment will be for a period of six months.

Applications, with copies of testimonials, stating age, should be forwarded as soon as possible to : THOS. CLAPHAM, Secretary.

Middlesex County Council.

MIDDLESEX COLONY, CERTIFIED INSTITUTION, SHENLEY, Near ST. ALBANS.

Applications are invited from registered medical practitioners, Male or Female, not liable for War Service, for the post of ASSISTANT MEDICAL OFFICER (B1).

Salary from £350 p.a. (if holding D.P.M. £400 p.a.) to £460 p.a., according to qualifications and experience (plus bonus, now £22 2s. p.a.), with meals, laundry, and furnished accommodation.

The appointment will be in a temporary capacity, and determinable by three months' notice on either side.

Applications, with copies of not more than three recent testimonials, should reach the undersigned before the 22nd September, 1943, and state earliest date when available for duty. A medical examination may be required.

C. W. RADCLIFFE, Clerk of the County Council.

Guildhall, Westminster, S.W.1.

Middlesex County Council.

RESIDENT ASSISTANT MEDICAL OFFICER (B1) for Orthopædic Department (Fracture A. Dept. E.M.S.) required at CHASE FARM HOSPITAL, Enfield, Middlesex. Applications invited from registered medical practitioners (including R and W practitioners holding B2 posts), preferably with experience in orthopædic work. R practitioners holding B1 posts ineligible unless rejected by R.A.M.C. Salary £400 p.a. by £25 to £475, plus war bonus. Board, lodging, and laundry. Whole-time duties, such as Council may require, under supervision of Medical Director. Appointment is for four years only, subject to medical examination and one month's notice.

Applications, stating age, nationality, qualifications, present post, and previous experience, enclosing copies of not more than three recent testimonials, to the undersigned. Application forms not provided. Closing date 18th September, 1943.

C. W. RADCLIFFE, "B3," Clerk of the County Council.

Middlesex Guildhall, Westminster, S.W.1.

Middlesex County Council.

NON-RESIDENT SURGEON (B1) required at CLARE HALL COUNTY SANATORIUM, South Mimms, Middlesex (560 Beds). Applicants must be registered medical practitioners with a higher degree or diploma in surgery and some experience in thoracic surgery. Commencing salary between £650 and £1000 p.a., according to experience. Additional cost-of-living bonus if salary under £850 p.a. A large amount of thoracic surgery is done at Sanatorium. Successful applicant would work as Assistant with Visiting Thoracic Surgeons and general scope of his duties would be arranged by Medical Director, but within these limits would have freedom in clinical action. Appointment is whole time, unestablished, subject to medical examination, and three months' notice. Post is non-resident, but surgeon appointed must live near Sanatorium. Salary is inclusive; any fees received must be paid to County Council.

Applications, stating age, nationality, qualifications, present post, and previous experience, enclosing copies of not more than three recent testimonials, to the undersigned. Application forms not provided. Closing date 18th September, 1943.

C. W. RADCLIFFE, "B3," Clerk of the County Council.

Middlesex Guildhall, Westminster, S.W.1.

Victoria Hospital for Children,

Tite-street, Chelsea, S.W.3.

Applications are invited from registered medical practitioners (Male and Female) for the appointment of RESIDENT MEDICAL OFFICER (B1) for a period of six months, vacant 16th October. Applicants should have held house appointments and had surgical experience. Salary is at the rate of £200 per annum. Suitably qualified R and W practitioners holding B2 appointments, also R practitioners holding B1 appointments and rejected by the R.A.M.C., may apply.

Also for the appointment of HOUSE PHYSICIAN (A), vacant 31st October next. Appointment is for a period of six months. Salary at the rate of £150 per annum. Practitioners within three months of qualification and liable under the National Service Acts may apply.

Applications should be sent not later than first post on Friday, 1st October, to: D. ST. JOHN BAMFORD, Secretary.

Bolingbroke Hospital,

Wandsworth Common, S.W.11.

Applications are invited from registered medical practitioners (Male) for the appointment of HOUSE SURGEON (A), vacant 1st October, 1943. Salary at the rate of £120 p.a., with full residential emoluments. Appointment is for six months. Practitioners within three months of qualification and liable under the National Service Acts may also apply.

Applications, stating age, nationality, qualifications, and experience, accompanied by copies of three recent testimonials, should be sent as soon as possible to—

W. S. RANDOLPH BISS, Secretary-Superintendent.

Miller General Hospital,

Greenwich High-road, S.E.10.

Applications are invited from registered medical practitioners for the appointment of CASUALTY OFFICER (Non-resident) (B1). Duties to commence as soon as possible. Salary is at the rate of £350, plus £100 per annum board allowance. Subject to acceptance by E.M.S. Suitably qualified R and W practitioners holding B2 appointments, also R practitioners holding B1 appointments and rejected by the R.A.M.C., may apply.

Applications, giving full details of age, experience, &c., must reach the undersigned not later than 21st September, 1943.

2nd September, 1943. L. G. BAIN, Assistant Secretary.

Borough of Willesden.

Applications are invited for the post of RESIDENT MEDICAL OFFICER (B2) at the WILLESDEN MUNICIPAL (FEVER) HOSPITAL. Salary at the rate of £250, plus bonus of £16 10s. for men and £13 0s. 6d. for women per annum, with board, lodging, and laundry, and the appointment will be subject to the Staff regulations of the Council. The Hospital admits all the notifiable diseases. R and W practitioners who now hold A posts may apply, when appointment will be limited to six months; otherwise may be extended to one year.

Applications, stating age, qualifications, nationality, and previous experience, with copies of three recent testimonials, to be sent to the Medical Superintendent, Willesden Municipal Hospital, Brentfield-road, Neasden, N.W.10, as soon as possible.

24th August, 1943. W. T. PIRIE, Town Clerk.

King George Hospital, Ilford.

Applications are invited from registered medical practitioners, Male and Female, for the appointment of RESIDENT ANÆSTHETIST (B2), vacant 1st October, 1943. The salary is at the rate of £350 per annum, with full residential emoluments. R and W practitioners who now hold A posts may apply, when appointment will be limited to six months.

Applications, with full copies of testimonials, should reach the undersigned by 17th September.

G. AUSTIN HEPWORTH, Secretary and Superintendent.

Anglesey County Council.

Applications are invited from duly qualified medical practitioners (Men or Women) for the temporary combined appointments of ASSISTANT COUNTY MEDICAL OFFICER, ASSISTANT SCHOOL MEDICAL OFFICER, MEDICAL SUPERINTENDENT of the VALLEY EMERGENCY HOSPITAL, and MEDICAL OFFICER of the VALLEY PUBLIC ASSISTANCE INSTITUTION. The person appointed must reside within a radius of three miles of Valley and devote his (her) whole time to the duties of the combined appointments. Salary £800 per annum (plus war bonus at present £24 per annum). Travelling expenses on the County scale.

Applications, stating age, qualifications, and experience, accompanied by copies of not more than three recent testimonials, should be received by the undersigned on or before 25th September, 1943.

WILLIAM JONES, Clerk of the County Council.

Shire Hall, Llangefni, Anglesey, August, 1943.

East Sussex County Mental Hospital,

HELLINGLY, near HAILSHAM, SUSSEX.

Required immediately, duly registered TEMPORARY ASSISTANT MEDICAL OFFICER (B1), Male or Female. Special experience in mental illnesses is not essential. Salary £8 8s. per week, with board, apartments and laundry. Suitably qualified R and W practitioners holding B2 appointments, also R practitioners holding B1 appointments and rejected by the R.A.M.C., may apply.

Applications, stating age, nationality and experience, to the MEDICAL SUPERINTENDENT.

Cheshire County Council.

WEST PARK (COUNTY) GENERAL HOSPITAL, MACCLESFIELD. (280 Beds.)

Application is invited from registered medical practitioners (Male or Female) for the appointment of RESIDENT ASSISTANT MEDICAL OFFICER (B1). Salary £350 per annum, with the usual residential allowances. Suitably qualified R and W practitioners holding B2 posts, also R practitioners holding B1 and rejected by the R.A.M.C., may apply.

Application to be made on forms obtainable from the undersigned and returned not later than the 22nd September, 1943.

IAN MACKAY, County Medical Officer of Health.

Public Health Department, 24, Nicholas-street, Chester.

Surrey County Council.

PUBLIC ASSISTANCE DEPARTMENT.

GROVE ROAD INSTITUTION, RICHMOND.
(260 Beds, mainly chronic sick.)

Applications are invited from registered medical practitioners, Male and Female, for the appointment of ASSISTANT MEDICAL OFFICER (B2). Salary £250 p.a., with full residential emoluments. R and W practitioners who now hold A posts may apply, when appointment will be limited to six months; otherwise will be for a period of one year.

Apply to COUNTY MEDICAL OFFICER, County Hall, Kingston-on-Thames.

Surrey County Council.

PUBLIC HEALTH DEPARTMENT.

ST. HELIER COUNTY HOSPITAL, CARSHALTON.
(862 Beds.)

APPOINTMENT OF HOUSE OFFICER (A).

Applications are invited from registered medical practitioners, Male and Female, for the above appointment. Salary is at the rate of £120 p.a., plus full residential emoluments. Practitioners within three months of qualification and liable under the National Service Acts may apply, when appointment will be for a period of six months; otherwise will not exceed one year.

Apply to MEDICAL SUPERINTENDENT.

Surrey County Council.

ST. HELIER COUNTY HOSPITAL, CARSHALTON.
(862 Beds.)

MATERNITY AND GYNÆCOLOGICAL UNIT.

Applications are invited from registered medical practitioners, Male and Female, for the appointment of JUNIOR ASSISTANT OBSTETRICIAN (B2). Salary £250 p.a., with full residential emoluments. R and W practitioners who now hold A posts may apply, when the appointment will be limited to six months; otherwise will be for a period of one year.

Apply to MEDICAL SUPERINTENDENT.

Corporation of Aberdeen.
PUBLIC HEALTH DEPARTMENT.

The Corporation of Aberdeen are prepared to receive applications for the post of LABORATORY ASSISTANT in the Public Health Laboratories at the CITY HOSPITAL, Aberdeen. Applicants should have general experience in pathological and bacteriological technique and should have special experience in diagnostic tests for venereal diseases and hæmatology. The salary attached to the post is £230, rising on approved service by annual increments of £10 to £250 per annum, with appropriate war bonus. The provisions of the Local Government Superannuation (Scotland) Act, 1937, shall apply to the appointment, and the person selected for appointment will be required to pass a medical examination before appointment.

Applications, stating age, present position, qualifications, and experience, together with copies of not more than three recent testimonials, should be lodged not later than 20th September current, with the City Bacteriologist, City Hospital, Aberdeen.

D. B. GUNN, Town Clerk.

Town House, Aberdeen, 1st September, 1943.

The Royal Liverpool United Hospital.
LIVERPOOL ROYAL INFIRMARY.

Applications are invited from registered medical practitioners for the B1 appointment of FIRST ASSISTANT to the ORTHOPÆDIC DEPARTMENT, duties to commence 1st October, 1943. Previous experience in orthopædic and fracture work is essential and the diploma of F.R.C.S. is desirable. Salary is at the rate of £350 p.a., non-resident. Suitably qualified R and W practitioners holding B2 appointments, also R practitioners holding B1 appointments and rejected by the R.A.M.C., may apply.

Applications, stating age, nationality, qualifications, with experience and details of previous appointments, and (except in the case of students of the Liverpool Medical School) accompanied by copies of three recent testimonials, should be sent not later than Friday, 24th September, 1943, to—

A. V. J. HINDS, Secretary.

The Royal Liverpool United Hospital, 66, Rodney-street, Liverpool, 1, 11th September, 1943.

County Borough of Middlesbrough.
PUBLIC HEALTH DEPARTMENT.

HEMLINGTON EMERGENCY HOSPITAL.

Applications are invited from registered medical practitioners for the appointment of ASSISTANT RESIDENT MEDICAL OFFICER (B2) at the above Hospital (500 Beds). Good experience is afforded in both medical and surgical work. The salary is at the rate of £300 per annum, together with full residential emoluments. The successful candidate will be required to pass satisfactorily a medical examination. R and W practitioners who now hold A posts may apply, when appointment will be limited to six months; otherwise it will be for a period of twelve months.

Applications to be sent to the Medical Officer of Health, Public Health Department, Municipal Buildings, Middlesbrough, not later than Tuesday, 21st September, 1943.

PRESTON KITCHEN, Town Clerk.

Municipal Buildings, Middlesbrough, 2nd September, 1943.

County Borough of Middlesbrough.
PUBLIC HEALTH DEPARTMENT.

WEST LANE ISOLATION HOSPITAL.

Applications are invited from registered medical practitioners, Male and Female, for the appointment of RESIDENT MEDICAL OFFICER (B1). The Hospital has 250 Beds, and experience is afforded in all forms of infectious diseases and tuberculosis. The successful candidate may also be required to undertake any other clinical duties in the Public Health Department as may be directed by the Medical Officer of Health, including assistance at Infant Welfare Clinics. The appointment is for an initial period of twelve months, the salary being at the rate of £350 per annum, plus full residential emoluments. The post is renewable after twelve months in which case the salary will rise by annual increments of £25 to a maximum of £450. The appointment is subject to the Council's Staff Regulations and will be terminable by one month's notice on either side. Suitably qualified R and W practitioners holding B2 appointments, also R practitioners holding B1 appointments and rejected by the R.A.M.C., may apply.

Applications should be endorsed "Resident Medical Officer" and sent to the Medical Officer of Health, Public Health Department, Municipal Buildings, Middlesbrough, not later than Tuesday, 21st September, 1943. PRESTON KITCHEN, Town Clerk.

Municipal Buildings, Middlesbrough, 2nd September, 1943.

Great Barr Park Colony and Hospital,
BIRMINGHAM, 22A.

Applications are invited from registered medical practitioners, Male and Female, for the appointment of ASSISTANT RESIDENT MEDICAL OFFICER (A), now vacant. Salary is at the rate of £275 per annum, with full residential emoluments, plus war bonus. Practitioners within three months of qualification and liable under the National Service Acts may also apply, when appointment will be for a period of six months; otherwise not exceeding one year.

Applications, stating age, qualifications with dates, and nationality, and accompanied by copies of three recent testimonials, should be sent to the MEDICAL SUPERINTENDENT, Great Barr Park Colony, Birmingham, 22A.

Surrey County Council.
NETHERNE HOSPITAL, COULSDON.

TEMPORARY ASSISTANT MEDICAL OFFICER (B1) (Male or Female) required. £450–£550 per annum, with full board and lodging, and an extra £50 for D.P.M. If married quarters are required, the emoluments might be replaced by cash. Applicants must be prepared to interest themselves in active forms of psychiatric treatment, though no previous experience is necessary. R and W practitioners now holding B2 posts, also R practitioners holding B1 and rejected by the R.A.M.C., may apply.

Apply, with copies of recent testimonials, to MEDICAL SUPERINTENDENT.

The Royal Infirmary, Worcester.
(Beds 341, including 131 E.M.S.)

Applications are invited from registered medical practitioners for the appointment of HOUSE PHYSICIAN (B2). Salary will be at the rate of £200 a year, plus full residential emoluments. R and W practitioners who now hold A posts may apply, when appointment will be limited to six months.

Applications, with copies of not more than three testimonials, should be addressed to—

HAROLD WIGG, Acting Superintendent-Secretary.

Manchester Hospital for Consumption
AND DISEASES OF THE THROAT AND CHEST.

Applications are invited from registered medical practitioners, Male and Female, for the appointment of RESIDENT HOUSE SURGEON (B2) at the ST. ANNE'S HOSPITAL, Bowdon, Cheshire, vacant 1st November. The Hospital has 50 Beds and the work is mainly ear, nose, and throat. Salary £250 per annum, with full residential emoluments. R and W practitioners who now hold A posts may apply.

Applications, stating age, qualifications, and nationality, and accompanied by copies of three recent testimonials, should be sent not later than 2nd October, 1943, to: W. HUNT, Secretary.

Manchester Hospital for Consumption, 45, Hardman-street, Manchester, 3.

Warwickshire King Edward VII
MEMORIAL SANATORIUM, HERTFORD HILL, Near WARWICK. (225 Beds—Pulmonary Tuberculosis.)

Applications are invited from registered Women medical practitioners, including W practitioners who now hold A posts, for the post of JUNIOR ASSISTANT MEDICAL OFFICER (B2). The appointment is for six months, subject to renewal for a further six months to other than W practitioners. Salary at the rate of £350 p.a., with full residential emoluments.

Applications to be sent by 20th September to—

Lt. EDGAR STEPHENS,
Clerk to the Joint Committee, Shire Hall, Warwick.

4th September, 1943.

Royal Devon and Exeter Hospital,
EXETER.

Applications are invited from registered medical practitioners (Male and Female) for the appointment of Two HOUSE PHYSICIANS (A), vacant 25th October next. Salary is at the rate of £160 per annum, with full residential emoluments. Practitioners within three months of qualification and liable under the National Service Acts may also apply, when appointment will be for a period of six months.

Applications will also be considered from students who expect to be qualified by the 25th October. One appointment is combined with House Surgeon to the Ear, Nose, and Throat Department. L. PARKHOUSE, Secretary.

Winson Green Mental Hospital,
BIRMINGHAM, 18.

TEMPORARY ASSISTANT MEDICAL OFFICER (B1), Man or Woman, required. Must be ineligible. Experienced psychiatrist preferred. Commencing salary £350 per annum, plus £50 to holder of the D.P.M., together with full residential emoluments valued at £80 per annum.

Applications to be sent to the MEDICAL SUPERINTENDENT on or before 25th September.

The Royal Portsmouth Hospital,
PORTSMOUTH.

Applications are invited from registered medical practitioners, Male and Female, for the appointment of HOUSE SURGEON (B2), vacant early October. The salary is at the rate of £200 per annum, with full residential emoluments. R and W practitioners who now hold A posts may apply. Six months' appointment.

Applications to be sent to: B. WAGSTAFF, Secretary.

Wrexham and East Denbighshire War
MEMORIAL HOSPITAL, WREXHAM.

Applications are invited from registered medical practitioners, Male and Female, for the appointment of HOUSE SURGEON (A), vacant 1st October, 1943. Salary is at the rate of £150 per annum, with full residential emoluments. Practitioners within three months of qualification and liable under the National Service Acts may apply. Appointment will be for a period of six months.

Applications to: LESLIE SPENCER, Secretary.

City of Plymouth.

CITY GENERAL HOSPITAL. (320 Beds.)

Applications are invited from duly qualified and registered medical practitioners, Male and Female, for the post of ASSISTANT MEDICAL OFFICER (B2). Salary will be at the rate of £300 per annum, plus a war bonus of £33 16s. for a male practitioner and £26 for a female, with full residential emoluments. All fees received by the officer must be refunded to the Council. The duties will be chiefly in the medical side of the Hospital. Further details of the post are obtainable from the Medical Superintendent of the City Hospital, Plymouth. R and W practitioners who now hold A posts may apply, when appointment will be limited to six months; otherwise it will be renewable for a further period of six months, terminable by one month's notice on either side.

Applications, stating age, nationality, and experience, together with copies of not more than three recent testimonials, should be sent as soon as possible to—

T. PEIRSON, Medical Officer of Health.

Seven Trees, Lipson-road, Plymouth.

City of Coventry.

The Coventry City Council invite applications from registered medical practitioners (Male or Female) for the temporary full-time post of ASSISTANT SCHOOL MEDICAL OFFICER AND ASSISTANT MEDICAL OFFICER OF HEALTH. The duties of the office are primarily in connexion with the medical inspection, &c., of school-children, but the officer appointed will also be required to assist if necessary in the general work of the Public Health Department. The salary will be at the rate of £600 per annum (plus war bonus at present £24 per annum), rising by annual increments of £25, £25, and £50 to £700, and the appointment will be terminable by one month's notice on either side.

Applications, stating age, qualifications, and experience, and enclosing copies of two recent testimonials, should be made as soon as possible to: FREDERICK SMITH, Town Clerk.

The Council House, Coventry.

The Bolton Royal Infirmary.

(245 Beds.)

Applications are invited from registered medical practitioners, Male and Female, for the appointment of HOUSE SURGEON (A), vacant 1st October, 1943. Salary £175 per annum, with full residential emoluments. Practitioners within three months of qualification and liable under the National Service Acts may also apply, when appointment will be for a period of six months.

Applications, stating age, nationality, and experience, together with copies of testimonials, to be forwarded to—

JOSEPH GRIFFITH, Superintendent-Secretary.

County Borough of Rotherham.

TEMPORARY ASSISTANT MEDICAL OFFICER OF HEALTH.

Applications are invited from duly qualified medical practitioners of either sex, who are not liable for military service, for the above post. Salary will be at the rate of £600 per annum, rising, subject to satisfactory service, by annual increments of £25 to £700 per annum, plus a temporary bonus amounting at present to £24 per annum. The duties will be chiefly in connexion with the School Medical and Maternity and Child Welfare sections, together with any other duties which may from time to time be allocated by the Medical Officer of Health. The post will be subject to the provisions of the Local Government Superannuation Act and to one month's notice on either side.

Application forms may be obtained from the Medical Officer of Health, Department of Health, Municipal Offices, Rotherham, and must be returned to the undersigned, accompanied by copies of three recent testimonials, not later than 30th September, 1943.

The consent of the Minister of Health has been obtained to this appointment. CHAS. L. DES FORGES, Town Clerk.

Municipal Offices, Rotherham, 31st August, 1943.

City and County of Newcastle upon Tyne.

SHOTLEY BRIDGE HOSPITAL.

HOUSE SURGEON (A) TO THE DEPARTMENT OF RADIOTHERAPY.

Applications are invited from registered medical practitioners, Male and Female, for the above post, vacant 23rd October. The successful candidate will also have opportunity of experience in medicine and surgery. The appointment is tenable for a period of six months, and the salary is at the rate of £150 per annum, with full residential emoluments. Practitioners within three months of qualification and liable under the National Service Acts are invited to apply.

Applications to be sent to the MEDICAL OFFICER OF HEALTH, Town Hall, Newcastle upon Tyne, 1.

Royal Surrey County Hospital,

GUILDFORD.

A vacancy exists on the Honorary Medical Staff of the Royal Surrey County Hospital, Guildford, for ASSISTANT PHYSICIAN for the duration, but the post will be advertised again after the war.

Applications, with not more than three testimonials, should be sent to the SECRETARY-SUPERINTENDENT by the 18th September, 1943.

Royal Lancaster Infirmary,

LANCASTER. (285 Beds.)

(Hospital recognised by the Royal College of Surgeons (England) for Two Senior Posts.)

Applications are invited for the following posts:—

SENIOR HOUSE SURGEON (B1), vacant 12th October. Salary £200.

SECOND HOUSE SURGEON (B2), Orthopædic, vacant 28th October. Salary £175.

SECOND HOUSE SURGEON (B2), Obstetrics and Gynæcology, vacant 22nd November. Salary £175.

JUNIOR HOUSE SURGEON (A), vacant 20th October. Salary £130.

HOUSE PHYSICIAN (A), vacant now. Salary £130.

In all cases full residential emoluments are included. For the B1 post, suitably qualified R and W practitioners holding B2 appointments, also R practitioners holding B1 appointments and rejected by the R.A.M.C., may apply. For the B2 posts, R and W practitioners who now hold A posts may apply. For the A posts, practitioners within three months of qualification and liable under the National Service Acts may apply. The appointments will be for the normal period of six months.

Applications, with testimonials, should be sent to—

N. L. SMITH, Superintendent-Secretary.

City of Manchester.

WITHINGTON HOSPITAL. (1150 Beds.)

(Recognised under the Regulations for the F.R.C.S.)

APPOINTMENT OF TEMPORARY RESIDENT ASSISTANT OBSTETRICAL OFFICER (B1).

Applications are invited from registered medical practitioners, Male and Female, for the above-mentioned post, vacant in October, 1943. The appointment will be temporary for the duration of the war. Candidates should have had previous experience in midwifery. The basic cash salary scale commences at £350 per annum and rises by annual increments of £25 to a maximum of £450, plus a temporary cost-of-living wages addition, with board, residence, and laundry in addition, subject to the Manchester Corporation conditions of service. Suitably qualified R and W practitioners holding B2 appointments, also R practitioners holding B1 appointments and rejected by the R.A.M.C., may apply.

Full information and forms of application may be obtained from the Medical Officer of Health, Hospitals Administration Section, P.O. Box No. 399, Town Hall, Manchester, 2, and applications for the post must be received by him not later than 25th September, 1943. Candidates for this vacancy who have completed forms of application in connexion with the similar vacancy at Crumpsall Hospital, Manchester, should inform the Medical Officer of Health accordingly without submitting a further application. Canvassing in any form is prohibited. R. H. ADCOCK, Town Clerk.

Town Hall, Manchester, 2, 2nd September, 1943.

Princess Elizabeth Orthopædic Hospital,

BUCKERELL BORE, EXETER.

(E.M.S. Fracture and Orthopædic Centre 1A—150 Beds with Annexe.)

Applications are invited from registered medical practitioners, including practitioners within three months of qualification and liable under the National Service Acts, for the post of HOUSE SURGEON (A). Salary £175 per annum, with board, residence, and laundry. The appointment is for six months.

Applications to: P. MELHUISH, Secretary.

Kent and Sussex Hospital,

TUNBRIDGE WELLS. (506 Beds.)

Applications are invited from registered medical practitioners (Male or Female) for the appointment of Two RESIDENT HOUSE SURGEONS (B2), vacant 30th October, 1943. Salary at the rate of £200 p.a., with full residential emoluments. R and W practitioners who now hold A posts may apply, when the appointment will be limited to six months.

Applications, with full particulars, to—

E. A. WAGSTAFF, Superintendent-Secretary.

31st August, 1943.

The Radcliffe Infirmary, Oxford.

Applications are invited from registered medical practitioners, Male and Female, for the appointment of OBSTETRIC HOUSE PHYSICIAN (B2), vacant 1st November, 1943. The appointment will be for a period of six months. Salary is at the rate of £100 per annum, with full residential emoluments. R and W practitioners who now hold A posts may apply.

Applications, stating qualifications with dates, age, and nationality, with copies of three testimonials, must be sent not later than Monday, 27th September, 1943, to—

A. G. E. SANCTUARY, Administrator.

The Royal Liverpool Children's Hospital,

Myrtle-street, LIVERPOOL, 7.

The Committee invite applications for the post of SURGICAL REGISTRAR (B1), for twelve months from 1st October, 1943. Salary at the rate of £125 per annum. Suitably qualified R and W practitioners holding B2 appointments, also R practitioners holding B1 appointments and rejected by the R.A.M.C., may apply.

Further particulars may be obtained from the SECRETARY of the Hospital, to whom applications should be sent, with copies of recent testimonials, by an early post.

Borough of Hove.

(AMENDED ADVERTISEMENT.)

TEMPORARY ASSISTANT MEDICAL OFFICER OF HEALTH AND ASSISTANT SCHOOL MEDICAL OFFICER.

Applications from suitably qualified Men or Women, preferably not liable for military service, are invited for the above appointment, due to the resignation of the present holder of the post. Salary £650 per annum, together with a car allowance of £50 per annum, determinable on either side by three months' notice. The post is subject to the Local Government Superannuation Act, 1937, and to the successful candidate, who will be precluded from engaging in private practice, passing a medical examination. The duties include work in connexion with the Public Health and School Medical Services, and also Civil Defence. Preference will be given to candidates having a knowledge of infectious diseases, including tuberculosis, and possessing the D.P.H. The consent of the Ministry of Health has been given to this appointment.

Applications, accompanied by full particulars of the candidate's qualifications and liability for military service, together with copies of three recent testimonials, should be sent to the Medical Officer of Health, Town Hall Annexe, Third-avenue, Hove, on forms to be obtained from him and returned as soon as possible. W. JERMYN HARRISON, Town Clerk.

City of Plymouth.

CITY GENERAL HOSPITAL.

Applications are invited from duly qualified and registered medical practitioners, Male and Female, including practitioners within three months of qualifying and liable under the National Service Acts, for the appointment of JUNIOR ASSISTANT MEDICAL OFFICER (A). The appointment will be for a period of six months, and terminable by one month's notice on either side. Salary is at the rate of £250 per annum, plus war bonus, with full residential emoluments. All fees received by the officer must be refunded to the Council.

Further details may be obtained from the Medical Superintendent. Forms of application are not provided. Applications must be addressed to the undersigned, together with copies of not more than three recent testimonials, as soon as possible.

T. PEIRSON, Medical Officer of Health.

Seven Trees, Lipson-road, Plymouth, 28th August, 1943.

King Edward VII Hospital, Windsor.

Applications are invited from registered medical practitioners Male or Female, for the appointment of HOUSE SURGEON (B1) in charge of IN- AND OUT-PATIENT CASUALTIES AND ACCIDENT SERVICE, vacant immediately It is desirable that applicants should hold the qualification F.R.C.S. Salary is at the rate of £300 per annum, with full residential emoluments. Suitably qualified R and W practitioners holding B2 appointments, also R practitioners holding B1 appointments and rejected by the R.A.M.C., may apply.

Applications, stating age, qualifications with dates, and nationality, together with copies of three recent testimonials, should be sent as soon as possible to: G. WESTON, Secretary.

Bodmin Emergency Hospital.

Applications are invited from registered medical practitioners, Male or Female, for the appointment of RESIDENT HOUSE SURGEON (B2). Salary is at the rate of £200 per annum, with full residential emoluments. R and W practitioners who now hold A posts may apply, when appointment will be limited to six months, otherwise not exceeding one year.

Applications, stating age, qualifications with dates, and nationality, and accompanied by copies of three (recent) testimonials, should be sent to the MEDICAL SUPERINTENDENT, Bodmin Emergency Hospital, Bodmin, Cornwall, as soon as possible.

West Suffolk General Hospital,

BURY ST. EDMUNDS.

(191 Civilian Beds, 244 E.M.S. and Reserve Beds.)

Applications are invited from registered medical practitioners for the appointment of HOUSE SURGEON (B2) to take charge of E.M.S. beds, for general and traumatic surgery. Experience in anæsthetics essential. Salary, with full residential emoluments, will be at the rate of £200 per annum. Practitioners now holding A posts (males must be rejected by the R.A.M.C.) may also apply, when appointment will be limited to six months; otherwise it will be for six months with a possibility of renewal at the pleasure of the Committee of Management.

Applications, stating age, nationality, qualifications, and accompanied by copies of testimonials, to—

27th August, 1943. E. E. HARDWICKE, Secretary.

Derbyshire County Council.

The Derbyshire County Council require the services of a fully qualified Whole-time WOMAN ASSISTANT MATERNITY AND CHILD WELFARE MEDICAL OFFICER with experience in antenatal work, midwifery, and children's diseases, to hold (under the direction of the County Medical Officer of Health) consultations at the Antenatal and Maternity and Child Welfare Centres of the Derbyshire County Council, and to perform such other duties as appertain to the office. The salary will be £600 per annum, rising by £25 per annum to £700 per annum, plus a war bonus, which at the moment is £24 per annum, with a travelling allowance in accordance with the County scale, which at present is as follows: cars of 8 h.p. and under, £70 per annum, plus 2d. per mile; cars of 9 h.p. and over, £75 per annum, plus 2½d. per mile. The post will be subject to the provisions of the Local Government Superannuation Act, 1937, and the successful candidate will be required to pass a medical examination. The appointment will be terminable by three months' notice on either side.

Forms of application may be obtained from the undersigned, to whom they should be returned not later than 18th September, 1943. The appointment is approved by the Ministry.

W. M. ASH, County Medical Officer of Health.

New County Offices, St. Mary's Gate, Derby,
27th August, 1943.

The University of Birmingham.

The Council invites applications for the newly established CHAIR OF SOCIAL MEDICINE. The appointment will carry an initial salary of £1500 per annum, but it is hoped that this will subsequently be increased to £2000 per annum. The successful applicant will be expected to commence his duties as soon as possible after the appointment has been made.

Further particulars of the appointment may be obtained from the undersigned, to whom applications (twelve copies) must be submitted, with the names of three referees, on or before 1st March, 1944. C. G. BURTON, Secretary.

The University, Edmund-street, Birmingham, 3.

Royal Albert Edward Infirmary and

DISPENSARY, WIGAN. (Normally 189 Beds.)

Applications are invited from registered medical practitioners for the appointment of RESIDENT MEDICAL AND SURGICAL OFFICER (B1), vacant 1st October, 1943. This post affords an excellent opportunity for improving surgical practice. Applicants should have held house appointments and had surgical experience. Preference will be given to candidates holding Diploma of F.R.C.S. Salary is at the rate of £250 per annum, plus war bonus. Suitably qualified R practitioners holding B2 appointments, also those holding B1 appointments and rejected by the R.A.M.C., may apply.

Applications, stating age, qualifications with dates, and nationality, and accompanied by copies of three recent testimonials, should be sent as soon as possible to—

A. STANLEY BRUNT, General Supt. and Secretary.

12th August, 1943.

City of Portsmouth.

SAINT MARY'S HOSPITAL. (1200 Beds.)

Applications are invited from Male registered medical practitioners for the appointment of JUNIOR RESIDENT MEDICAL OFFICER (A), vacant 18th September. The salary is at the rate of £250 per annum, with residential emoluments valued at £150 per annum, and a temporary cost-of-living bonus, at present payable at the rate of 6s. 6d. per week. Practitioners within three months of qualification and liable under the National Service Acts may also apply, when appointment will be for a period of six months; otherwise for twelve months.

Application forms may be obtained from, and must be returned to, the Medical Officer of Health, Northern Secondary School, Mayfield-road, Portsmouth.

FREDERICK SPARKS, Town Clerk.

Municipal Offices, Royal Beach Hotel, Southsea,
23rd August, 1943.

Gravesend and North Kent Hospital.

Applications are invited from registered medical practitioners, Male, for the appointment of HOUSE SURGEON (A), now vacant. Salary is at the rate of £175 p.a., with full residential emoluments. Practitioners within three months of qualification and liable under the National Service Acts may also apply, when appointment will be for a period of six months.

Applications should be addressed to the SECRETARY-SUPERINTENDENT.

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WAR MEMORIAL HOSPITAL,
High-lane, TUNSTALL, STOKE-ON-TRENT.

Applications are invited from registered medical practitioners, Male and Female, for the appointment of a HOUSE SURGEON (A), vacant immediately. Salary is at the rate of £175 per annum, with full residential emoluments. Practitioners within three months of qualification and liable under the National Service Acts may apply, when the appointment will be for a period of six months.

Applications to: C. E. LOWNDES, Secretary.

Hull Royal Infirmary.

Applications are invited from registered medical practitioners for the post of CASUALTY OFFICER (A), vacant September. Salary £200 per annum, with full residential emoluments. Practitioners within three months of qualification and liable under the National Service Acts may also apply, when appointment will be for a period of six months.

Applications should be addressed to—
R. J. CARLESS, House Governor.

The Royal Hospital, Wolverhampton.

(Incorporated under Royal Charter.) 310 Beds.

Applications are invited from registered medical practitioners, Male, for the appointment of HOUSE SURGEON (B2), FRACTURE AND ORTHOPÆDIC DEPARTMENT, now vacant. Salary is at the rate of £150 per annum, with full residential emoluments. R practitioners who now hold A posts may apply, when appointment will be limited to six months.

Applications to be sent to W. COCKBURN, House Governor.
19th July, 1943.

The Bolton Royal Infirmary.

(245 Beds.)

Applications are invited from registered medical practitioners, Male and Female, for the appointment of HOUSE PHYSICIAN (B2), vacant 29th September, 1943. Salary £200 per annum, with full residential emoluments. R and W practitioners who now hold A posts may apply, when appointment will be limited to six months.

Applications, stating age, nationality, and experience, together with copies of testimonials, to be forwarded to—
JOSEPH GRIFFITH, Superintendent-Secretary.

General Hospital, Nottingham, and

NOTTS BRANCH OF THE BRITISH EMPIRE CANCER CAMPAIGN.

A MEDICAL OFFICER required for the RADIUM AND DEEP X-RAY THERAPY DEPARTMENTS. Full time, non-resident. Salary £1000 to £1200 per annum, according to experience.

Applications, stating age, qualifications, and experience, together with copies of testimonials, to be sent to—
H. M. STANLEY, House Governor and Secretary.
General Hospital, Nottingham.

County Borough of Preston.

SHAROE GREEN HOSPITAL. (250 Beds.)

Applications are invited from registered medical practitioners, Female, for the appointment of JUNIOR RESIDENT MEDICAL OFFICER (A), vacant 1st October, 1943. Salary is at the rate of £150 per annum, with full residential emoluments. W practitioners within three months of qualification and liable under the National Service Acts may also apply, when appointment will be for a period of six months; otherwise not exceeding one year.

Applications, stating age, qualifications with dates, and nationality, and accompanied by copies of three recent testimonials, to the MEDICAL SUPERINTENDENT, Sharoe Green Hospital, Fulwood, Preston.

The Ministry of Health invite applications

from registered medical practitioners who intend to take up RADIOLOGY as a career and are prepared to enter for the examination during the winter of 1944–45. Applicants must have held appointments as House Officers for at least six months, and preference will be given to those who are unfit for war service and under thirty years of age. Successful candidates will be enrolled in the E.M.S. at £200 or £350 a year, according to length of qualification and hospital experience. If board and lodging are not provided an addition of £100 a year will be granted in lieu.

Applications should be sent to DIRECTOR OF ESTABLISHMENTS, Ministry of Health (Room 162), Caxton House West, Tothill-street, S.W.1, and should be accompanied if possible by a recommendation from the Dean of the Medical School at which they received their training stating that the candidate is in his opinion a suitable practitioner to undertake a course of Radiology.

Those selected in the first instance will be interviewed by representatives of the Ministry of Health, including the Consultant Adviser in Radiology, before a final decision is made.

Doctors, Male and Female, required

for duration Locums, Locums, and Assistantships, with or without view, in Yorkshire, Lancashire, Wales, &c. Good salaries paid. Vacancies for Hospital Locums and Ships' Surgeons.—Write A. SHAW, Medical Agent, Premier Buildings, 88, Church-street, Liverpool, 1.

Temporary Medical Officer (Female)

required for factory in the South of Scotland. Previous experience in industry will be considered an advantage but is not essential. Remuneration according to qualifications, approximately £700 per annum.—Applications, giving full particulars of training and experience, should be sent to Address, No. 320, THE LANCET Office, 7, Adam-street, Adelphi, London, W.C.2.

Imperial Chemical Industries Limited

require the services of a FEMALE WORKS MEDICAL OFFICER for a temporary period. Total emoluments will be according to qualifications.—Applications, with copies of not more than three recent testimonials, should be addressed to Staff Department, I.C.I. (Explosives) Ltd., Nobel House, Stevenston, Ayrshire.

Assistantship with view Partnership or

Succession wanted by ex-R.A.M.C. Scot. Married, experienced G.P. No midwifery. Not rural.—Address, No. 319, THE LANCET Office, 7, Adam-street, Adelphi, London, W.C.2.

Young Lady requires a position as

SECRETARY-CHAUFFEUSE to a Doctor, preferably in or near London, but will consider farther away.—Mrs. Southwell, 131, Stapleton Hall Road, London, N.4.

Reception Area.—Exceptional opportunity

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attractive house in County Town, South Scotland. Death vacancy, but income (about £700 net per annum) protected for period of war by pooling agreement entered into by all doctors in the town.—Address, No. 323, THE LANCET Office, 7, Adam-street, Adelphi, London, W.C.2.

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Medical Practices and Partnerships

for disposal, in Lancashire, Yorkshire, North Wales, &c. Town and country.—Write A. SHAW, Medical Agent, Premier Buildings, 88, Church-street, Liverpool, 1.

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reclaiming in accordance with Ministry of Supply requirements. Good prices paid for all quantities exceeding 10 lb. Send to MOROL LTD., 21, Woodthorpe-road, Ashford, Middlesex. Larger quantities, collection arranged.

Watson Service Microscope in excellent

condition, two eye-pieces, 2/x6 and 4/x10. Three objectives, 1/6, 2/3, 1/12, oil-immersion with brass container, substage condenser with adjustable diaphragm. The whole complete in mahogany cabinet. Price £30.—Address, No. 321, THE LANCET Office, 7, Adam-street, Adelphi, London, W.C.2.

Stamps for Sale.—Large stock of all

issues of Colonials, including current high values used, also foreign; selections to responsible applicants sent on request. Highest prices for stamps of all kinds in small or large lots.—P. LEWIS, B.P.A., 12½, Grocers Hall-court, Poultry, E.C.2.

Expert advice given on Insurance.

All classes of Insurance transacted.—For further particulars write A. SHAW, Medical Agent, Premier Buildings, 88, Church-street, Liverpool, 1.

Financial Assistance can be arranged

for the purchase of Medical Practices and Partnerships.—For further particulars write A. SHAW, Medical Agent, Premier Buildings, 88, Church-street, Liverpool, 1.

Comfortable accommodation required

for elderly lady in house of Doctor or Nurse in London or Home Counties recovering from nervous breakdown. Nursing attention required.—Address, No. 322, THE LANCET Office, 7, Adam-street, Adelphi, London, W.C.2.

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100 mgms. of radium element made up to any required specification, for the moderate fee of £5 5s., from—
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